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ARCHIVES OF PEDIATRICS

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DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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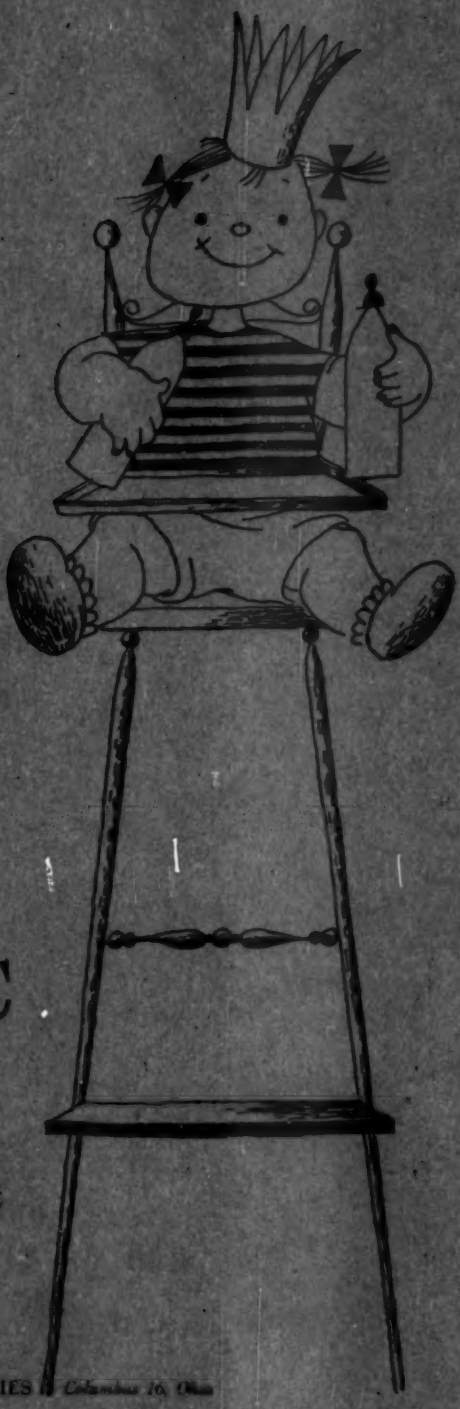

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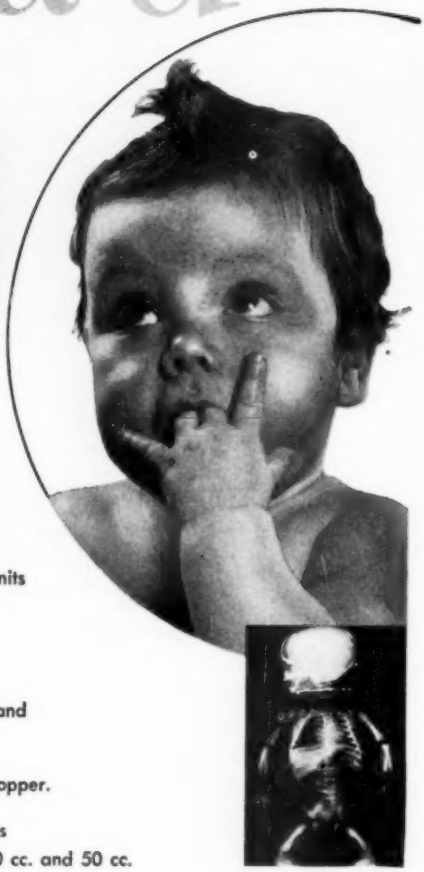

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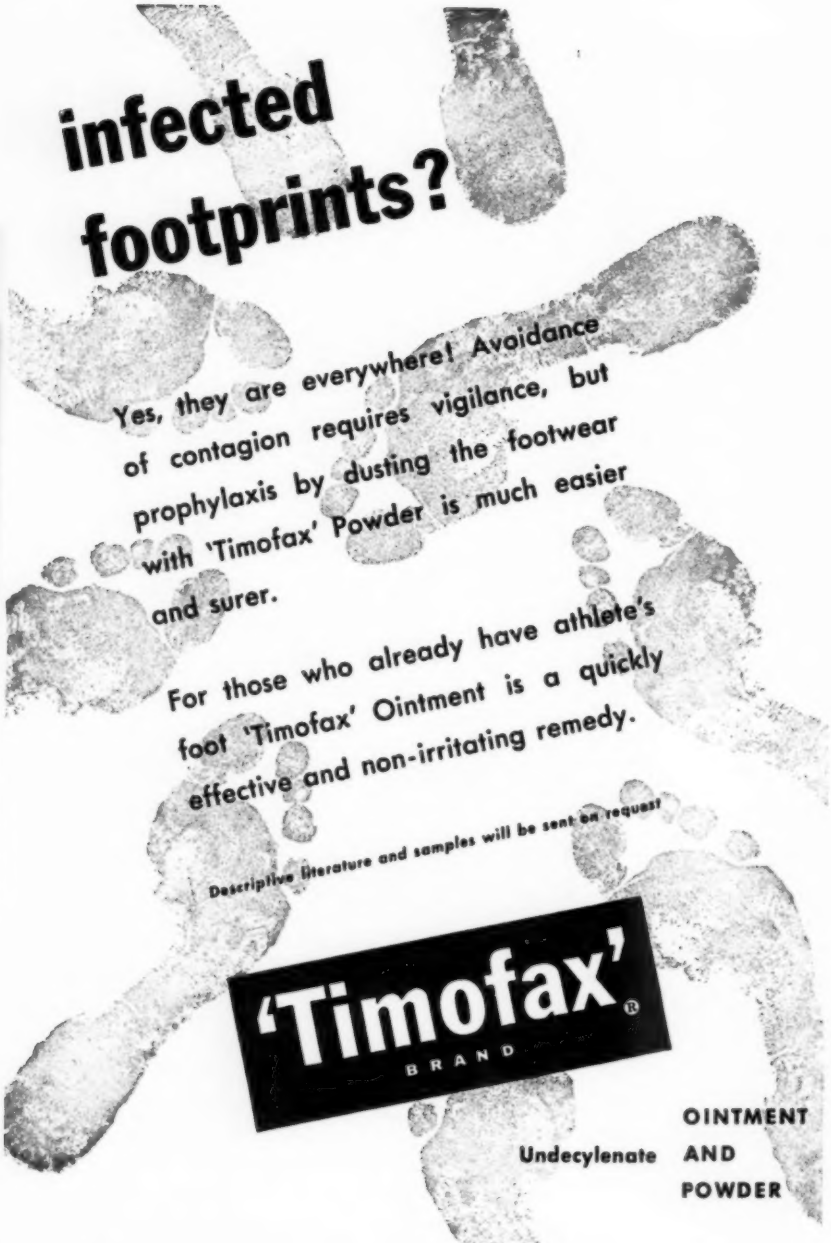

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ACUTE IRON POISONING*

REPORT OF A CASE AND REVIEW OF THE LITERATURE

JAMES W. MURPHY, M.D.
CHARLES NEUSTEIN, M.D.
A. C. HOFFMAN, M.D.
HAROLD V. WINTERS, M.D.
AND
ALBERT L. GASKINS, M.D.
Brooklyn.

Although in wide use as a hematinic, ferrous sulfate has been generally considered harmless by the oral route, except for occasionally producing nausea, abdominal pain, constipation and diarrhea[1, 2]. The amount of gastric irritation seems to depend on the solubility of the iron preparation, as does the utilization. Special coatings, designed to prevent solubility in the stomach, have been developed to lessen minor gastric irritation in the tablet form. Very little attention has been directed to the more severe toxic potentialities of ferrous sulfate.

Hurst[3] in Boston had a case of encephalopathy following large oral doses of iron and ammonium citrate (11 Grams per day for 3 weeks). Brock and Hunter[4] gave doses of 5-8 Grams per day and Blaud's pills (6 Grams a day) for 9 days, to children 7 to 14 years of age with no mention of toxicity. Reznikoff[5] gave a normal man iron and ammonium citrate in amounts equivalent to 2.0 Grams of metallic iron a day, without toxicity.

*From the Cumberland Hospital Pediatric Service of Dr. Thurman B. Givan, Brooklyn, N. Y.

In 1947, two fatal cases of ferrous sulfate poisoning were reported by Forbes[6], one in a three-year-old child, and the other in a one-year-old infant. They swallowed 50 tablets and between 30-35 tablets, respectively, of a preparation containing ferrous sulfate 0.2 Grams, copper sulfate 2.6 milligrams and manganese sulfate 2.6 milligrams per tablet. Both children developed signs and symptoms of gastro-intestinal irritation, restlessness, coma and shock. The first case was featured primarily by vomiting and icterus; the second by hematemesis. The older patient lived 53 hours and the younger patient 30 hours.

Thomson[7] reported a fatality with respiratory distress of a 16-month-old infant who ingested 26 tablets of a similar preparation of ferrous sulfate. He also records a survival in a 2-year-old child who swallowed 10 tablets of the same preparation, with occult blood detectable in the stool nine days later.

Also in 1947, Prain[8] reported a fatality in an 11-month-old infant who swallowed an unknown quantity of tablets containing iron, copper and manganese. She died 39 hours later, after a period of apparent well-being. Lindquist[9] reported a nonfatal case of ferric chloride poisoning in a 2½-year-old girl, with hematemesis, bloody stool and collapse. Smith, Jones and Cochran[10] report a single fatal case of iron poisoning. They suggest that the gray cyanosis noted in their case was probably due to methemoglobinemia because of definite improvement of the cyanosis after methylene blue therapy.

Thomson[11] reviewed six cases at the Dundee Royal Infirmary, including 2 fatalities previously recorded[7, 8], for the five-year-period from 1944 to 1949. The prominent findings in the four cases that recovered were pallor, drowsiness, vomiting and the passage of dark brown to black stools.

The following patient is of interest in that, unlike most previously reported cases, she demonstrated toxicity to a large amount of ferrous sulfate alone, surviving an amount bordering on the fatal dose[12].

CASE REPORT

A 30-month-old white female child was admitted to Cumberland Hospital on June 22, 1950, at 10:20 P.M., because of "vomiting and gagging".

One day prior to admission, the patient's mother had donated

blood and was given 100 tablets of ferrous sulfate (0.2 Grams per tablet) in an envelope. At 1 P.M. the day of admission the mother noticed the child sucking the tablets. The child was not near any window, sink, refuse-can or bathroom where she might have discarded some of the tablets. After a careful search only 25 tablets were recovered from the floor and envelope. At 5 P.M. (4 hours after ingestion) the child began to vomit blood-tinged material. The vomiting recurred four or five times and was associated with the passage of two to three diarrheal stools. The past history was non-contributory. The family history revealed that the mother had had infectious hepatitis during her sixth month of pregnancy.

On admission the physical examination was that of a well-developed, well-nourished, pale child who was playful, alert, interested in her surroundings, and who did not appear acutely ill. The pulse was 150, the temperature 99° F. (37.2° C.), respiration 16, blood pressure 96/50 and weight 11.7 Kg. The heart, lungs, abdomen, extremities and neurologic examinations were all normal. The only positive findings were a mild tonsillitis and pharyngitis.

The stomach was lavaged with 1,500 cc. of normal saline. The initial returns were grossly bloody but subsequent returns were clear. Vomiting occurred during the lavage, but no tablets were returned. The patient was treated with sodium bicarbonate, aluminum hydroxide gel, and penicillin in oil. After the first dose of sodium bicarbonate, the patient vomited approximately 100 cc. of pinkish fluid with particles of blood dispersed throughout the vomitus. There was no further vomiting during the patient's hospital stay. The temperature never rose higher than 99.8° F. (37.7° C.). The child had a fair appetite and took a normal diet after the first 24 hours during which time she was on a milk regime. Stools were normal after the passage of two tarry stools within the first 24 hours.

The child remained alert and playful throughout her period of hospitalization and showed no evidence of hepatic or renal injury. At no time did she appear very ill. The laboratory reported normal findings on repeated urine examinations, except for a 1 plus sugar in the first specimen. Complete blood counts on June 23 and 28, 1950 were reported as hemoglobins of 86 per cent and 78 per cent, red blood cells 4.3 million and 4.0 million, white blood cells 16,000 and 10,800. Blood differential smears showed

polymorphonuclear cells 63, lymphocytes 32, monocytes 5 and polymorphonuclear cells 50, lymphocytes 46, eosinophiles 4, respectively. Stool examination on June 23, 1950 was negative for occult blood. Kline test was negative. Phenolsulfonphthalein test on June 30, 1950 was negative. Liver function tests were reported as icterus index 5 units, Takata ara and cephalin flocculation negative. All were done on June 28, 1950. Roentgen examination on June 23, 1950 was reported as chest entirely normal, abdomen showed moderate gaseous distention of the stomach and a normal amount of gas throughout the intestinal tract, no evidence of tablets.

The patient made an uneventful recovery and was discharged on July 2, 1950, 11 days after admission.

DISCUSSION

The main features observed in this patient were pallor, hematemesis and tarry stool. This is in agreement with the findings reported by the British authors. Our patient presented no clinical or laboratory evidence of hepatic failure as was noted in the fatal cases reported by them.

On postmortem examinations of the few reported cases all showed edema and necrosis of the gastric mucosa, with congestion and hemorrhagic areas between the muscle layers. Prain[6] noted thrombosis of the submucosal veins under the necrotic areas of the gastric mucosa, with iron impregnated in the walls of the veins. Deeper veins that were not thrombosed showed thickened endothelium with masses of iron granules present. The changes in the liver varied from cloudy swelling to focal necrosis[6] with some iron demonstrable. The kidneys may show cloudy swelling and there may be necrosis of the malphighian corpuscles of the spleen.

The extent of the pathology found on the postmortem examinations seemed inadequate to explain the cause of death. Whether death is due to the absorbtion of iron into the general circulation or whether it is due to shock from tissue damage with absorbtion of the toxic products of necrosis has not been ascertained, although the extent of liver damage is usually not severe. Prain suggests that death follows collapse of liver function. He assumes that the damaged liver is capable of functioning well for some time, but cannot continue its detoxifying action in the presence of continued absorbtion of toxic products. The collapse of the liver permits the

distribution of toxic substances to the rest of the body, terminating in sudden death.

Following the reports of fatal cases from excessive ingestion of ferrous sulfate tablets by Forbes and Thomson[6, 7], Somers[12] investigated the relative oral toxicity of various therapeutic iron preparations. Using mice, rabbits and guinea pigs as subjects, it was found that ferrous sulfate, ferrous gluconate, and iron and ammonium citrate had the same toxicity. There was no difference in the toxicity of ferrous sulfate when copper and manganese were added to the preparation. Ferric iron preparations were found to be up to twice as toxic as ferrous preparations. No adequate explanation for this finding is presented in view of the fact that ferric iron is reduced in the stomach to the ferrous state. Blaud's pills were found to be one-fourth as toxic as the other preparations but also had a lower therapeutic value. This is apparently due to the relative insolubility of ferrous carbonate in gastric and intestinal contents. Clinically, the animals became prostrated within a few minutes after the oral administration of a toxic dose of iron. Reflexes became sluggish or disappeared, respiratory rate was increased, coma ensued, and death occurred within two to six hours. Postmortem examinations showed findings similar to those seen in humans, with no obvious cause of death.

The results obtained with Blaud's pills suggested the possible usefulness of sodium carbonate or bicarbonate as an antidote. Somers[12] therefore gave four rabbits known toxic doses of ferrous sulfate (3 Grams per Kilogram of body weight) and similar doses of sodium carbonate to two of the rabbits. One of these rabbits lived for two days and the other recovered completely. The two rabbits who did not receive sodium carbonate died overnight. The experiment was repeated twice with similar results.

Thomson[11] stresses the following features in the management of acute ferrous sulfate poisoning: (1) Emesis may be successful in ridding the body of swallowed tablets up to one hour after ingestion. (2) Gastric lavage should be performed with an aqueous bicarbonate solution to convert the corrosive ferrous sulfate to the much less irritant ferrous carbonate and to dilute the poisonous substance. (3) Bismuth preparations should be administered orally in order to protect the gastric mucosa. This measure is to prevent sudden fatal collapse possibly due to toxic absorbtion from dam-

aged mucous membranes after a period of apparent improvement.

Roxburgh[13] reported a case of iron poisoning with recovery in a 16-month-old male infant. Dimercaprol (BAL) was administered daily for three days, but the author made no claim for its value. Treatment of iron poisoning with dimercaprol has been disappointing in animals[14]. The use of BAL seems to aggravate the effects of ferrous sulfate and ferric chloride, and a BAL-iron complex seems to be formed that is more toxic than the corresponding amount of iron salts alone.

Smith, Jones and Cochran[10] suggested that methemoglobin studies be done in these cases, and that they be treated with methylene blue if methemoglobinemia is found to be a factor.

SUMMARY

A case of ferrous sulfate toxicity in a child is reported and a brief review of the literature presented. Our patient developed marked gastric irritation with hematemesis following the ingestion of 15 Grams of ferrous sulfate (1.28 Gram per Kilogram). Unlike most of the previously reported cases there were no demonstrable systemic effects from ferrous sulfate alone. The potential danger of leaving iron preparations within the reach of children is illustrated. Possible methods of treatment are discussed.

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IODINE IN THE TREATMENT OF POLIOMYELITIS AND OTHER PARALYTIC DISEASES

RALPH R. SCOBEY, M.D.
Syracuse, N. Y.

At the present time, the treatment of poliomyelitis is admittedly symptomatic. It appears pertinent, therefore, that any remedy that has been shown to be more or less effective in this disease be given thoughtful consideration. Iodine, of all the drugs that have been reported in the literature for years, appears to have been more effective than any other in the treatment of poliomyelitis. This fact is evidently not fully appreciated by many contemporary physicians.

It is the purpose of this report, therefore, to consider the use of iodine in poliomyelitis and other paralytic diseases and to note the results obtained with it by a number of workers. Cooke,[1] England, (1824) made the following pertinent remark and it is obviously applicable today: "It was the opinion of a late eminent physician, that more real service may be rendered to medicine by the illustration of what is already known on the subject, than by any attempts to promulgate new theories or new modes of practise."

REPORTS OF IODINE THERAPY IN POLIOMYELITIS

Manson,[2] England, (1825) in his book, "Medical Researches on Effects of Iodine in Bronchocele, Paralysis, Chorea, Scrofula, Fistula Lachrymalis, Deafness, Dysphagia, White Swelling and Distortions of the Spine," devotes 102 pages to the use of iodine in paralysis.

Manson says: "The different species of Palsy occur so frequently, and, in the great majority of cases, are so difficult to cure, that any remedy that can effect so desirable an object, or even relieve a portion of the unfortunate individuals who labour under so severe an affliction, will, I flatter myself, be acceptable to the medical world; for, notwithstanding, the great attention that has of late years been given to the Pathology of Palsy, and although various new remedies have been employed and recommended by ingenious men for its cure, still we must admit the melancholy fact, the Palsy generally proves an obstinate and untractable disease, too often baffling all our plans, and resisting our most potent remedies.

"It was want of success with the remedies usually employed, in much slighter cases of Palsy than the deplorable one I am about to detail, that led me to try a new method of curing the disease.

"The wonderful powers of iodine, which I had recently witnessed, and a long previous acquaintance with the effects of the same remedy, as it exists in burnt sponge in reducing morbid enlargements of the Thyroid gland, led me, from analogy, to think, that in cases of Palsy, from tumors, or fluids, pressing on the brain, or spinal cord, or from morbid thickening of the investing membrane of the cord itself, Iodine might prove a useful remedy, not only stimulating the nervous system and removing tumefaction and effusion, but also by correcting the strumous state of the constitution that often gives rise to the disease."

Manson's reports are remarkable in view of the fact that they were published 83 years before the discovery of the virus of poliomyelitis and 14 years after the discovery of iodine. Today, iodine is known to be a virucide. Manson claimed priority for the use of iodine in paralytic cases and describes its use in a severe case.

He states regarding this patient: "As the patient had been under the care of an able physician and experienced surgeon, for several months, without experiencing any benefit from the remedies employed, I conceived that it would be losing valuable time, and of no avail to the patient, to follow the usual routine of practise in so inveterate a case; on the contrary, I conceived myself called upon by every feeling of humanity, to use any means, that afforded a ray of hope, of alleviating the miserable situation of the poor sufferer."

Briefly Manson's case report, in his own words as far as possible, is as follows: "James Watterton, aet. 19, was admitted an inpatient of the General Hospital, near Nottingham, on the 27th of March 1821. Has been ailing since October, 1819. Says he was attacked with pain in the bowels and griping. After some time the pain left the bowels, and the lower extremities became swollen and painful. His mother put his feet and legs in warm water, and after this, his neck became stiff and painful, and he began to be troubled with pains shooting from the neck into the left side of the head. . . . Almost immediately of the pain leaving him he lost the power of moving the left arm, and in a short time after the lower extremity of the same side became paralytic. Sometime after

this he recovered the use of the left arm in a considerable degree, the lower extremity of the same side remaining paralytic, and the right half of the body, as high as the neck, was seized instantaneously with complete palsy. He has continued in this wretched state, and has been getting worse, he thinks instead of better, and passes his stools and urine involuntarily. . . . He lies in bed on his back, and is completely palsied on both sides, from neck downwards, with the exception of the left upper extremity, over which he still has so much power as to be able to raise his hand as high as his chin, but he cannot grasp anything with the hand. The sense of feeling is very much impaired, but not quite obliterated in the paralytic parts. There is no distortion of the face, and the patient can articulate very well. Is troubled with twitchings of the lower extremities."

Tincture of iodine 10 gtt. t.i.d. in water, was prescribed on April 4 and on the 6th the patient could move the right arm a little and felt better. The iodine was increased to 15 gtt. t.i.d.

On April 9, the patient could raise the right arm to the head. The twitchings of the lower extremities had ceased. When placed in a sitting position in bed, he could support himself better than when admitted to the hospital. The iodine was increased to 20 gtt. t.i.d.

On April 10, he first recovered the use of the lower extremities so as to be able to move them a little, and he could bend the left leg a little upon the thigh. He now had power over the left arm, and moved it about with great freedom. He could hold his urine. He felt better and stronger.

On April 14, the patient continued to improve. He could now raise the left hand above his head, and move it around in all directions. The iodine was increased to 25 gtt. t.i.d.

On April 16, the paralytic symptoms continued to yield to the powerful influence of the iodine. When his meat is cut he can feed himself with the left hand. Can raise the right hand to the chin, and can draw the right lower extremity up towards the body, and raise it about two inches from the bed. The iodine was increased to 30 gtt. t.i.d.*

*After taking thirty drops of tincture of iodine thrice daily, for five days, the patient developed headache and his pulse was increased in frequency. The iodine was omitted and these symptoms disappeared. A smaller dose, 15 drops three times a day which was gradually increased, did not afterwards disagree with the patient.

On May 7, the patient was able to walk from his bedroom to the day-ward with very little assistance.

On July 2, he had complete use of all his limbs, and the sense of feeling as perfect as ever, according to Manson.

"July 3, Discharged cured."

Manson gives 25 other case histories with various manifestations of paralysis. Some of these were undoubtedly poliomyelitis. The results with the iodine treatment in the majority of these cases was equally as effective as that observed in the above case. Manson warns his colleagues as follows: "To the younger members of the profession, who may read this work, I beg to observe, that if they expect, by the exhibition of Iodine, to cure every case of the different diseases in which it has been decidedly useful, they will be much disappointed, as it is impossible for that, or any other medicine, to be invariably efficacious. For example, I find, from practise, that Iodine is greatly superior to any other remedy we possess, in the different species of Palsy; but I also know from experience, confirmed by dissection, that it will not cure that disease, when it arises from softening of the brain, or any other considerable disorganization of this most important organ, and, therefore, beg to caution them against rejecting a remedy as useless and inefficient, before giving it a fair and unprejudiced trial, in a sufficient number of cases; and if they will do so, I am quite certain that in the great majority of them, if taken in time, the medicine will recommend itself more powerfully and convincingly than I am able to do, as personal experience must always carry home deeper conviction, than a detail of facts by any practitioner."

Coplan[3] (1850) states: "I have prescribed iodine and the iodides in several cases of the various forms of partial and general palsy; but in no case of the disease have I ventured to employ them otherwise than in very small doses at first, carefully watching their effects, and cautiously increasing the doses. . . . Dr. Manson employed only the tincture; but, both before and after the publication of his cases, I had used both this and the iodide of potassium for this disease, as well as for some others, in public and private practise; and more recently the iodides—the iodides of potassium and the iodides of mercury—more frequently than the pure iodine. The preparations, especially the last, are best suited to the more chronic

and asthenic cases, or after depletions and other evacuants have been pushed sufficiently far. Even then the pulse should be at first small, and the effects upon the pulse carefully watched. The occurrence of headache ought to cause interruption in the use of these medicines. The iodide of potassium may be conjoined with liquor potassae and sarsparilla, commencing only with one or two grains, and gradually increasing it. I have even given one grain in twenty-four hours with advantage."

Brown-Séquard[4] (1861) recommended iodide of potassium as the only known remedy that may be employed without danger in the various forms of paraplegia, being especially useful in cases of white softening of the spinal cord caused by fatty degeneration of the blood vessels of that organ.

Sinkler[5] (1878) pointed out that iodide of potassium may be administered to advantage in the palsies of children. He noted that when he gave large doses of this drug for controlling attacks of asthma in an adult with poliomyelitis that it aided in improving the condition of the cord. He prescribed up to 100 grains daily. The patient was improved but not cured.

Elliot[8] (1885) states that a great variety of drugs have been used and recommended in the treatment of anterior poliomyelitis. Iodide of potassium has been most often employed and the most praised, he says. He described a case in which iodide was used in combination with ergot, counter irritation and rubbing of the limbs, commencing at about the sixth week. The result was immediately favorable. The use of potassium iodide by other clinicians is mentioned by Elliot. Erb[6] administered it internally, and dry cups and cold compresses were applied externally in a case of anterior poliomyelitis, two months after the first symptoms appeared. The patient soon commenced to improve and ultimately nearly recovered. In one of Charcot's cases[6] great improvement resulted in three months with the use of iodide of potassium internally and moxas to the spine. Soulier[6] employed iodide of potash with belladonna and the actual cautery at the end of three weeks in a case of poliomyelitis. This treatment resulted in complete recovery at the end of three months. Hammond[6] reported a case of a man of 35 years, who, on the fourth day of the disease, commenced to take iodide of potassium and ergot. The paralysis increased up to

the seventh day but improvement commenced on the ninth day. Afterwards electricity was employed, and at the end of a year no weakness remained.

Webber[7] (1885) in his book on nervous diseases recommends iodide of potassium in large doses in acute anterior poliomyelitis.

Jacobi[8] (1886), in her classical treatise on "Infantile Spinal Paralysis," also recommends the use of iodide of potassium in large doses in this disease. She states: "The action of this drug upon inflammations of the nerve-centers seems, within certain limits, to be indisputable, but its action is certainly very obscure. When the lesion can be attributed to a meningo-myelitis, the iodide may be expected to facilitate the absorption of the exudate."

In 1886, Eskridge[9] reported the case of a man, about 45 years of age, with gradually ascending paralysis for about three weeks. The patient completely recovered under potassium iodide.

Ridley[10] (1925) employed tincture of iodine with outstanding results in the treatment of beriberi, a paralytic disease which is genetically related, according to Braddon,[11] to poliomyelitis. Ridley found that three doses, five drops of the tincture once a day, completely cured an attack. He learned that the Dutch in the East Indies had been accustomed to administer iodine internally in the treatment of beriberi.

In 1927, Sir Thomas Horder[12] reported the use of colloidal iodine intravenously in the treatment of poliomyelitis. He advised that it be employed as early as possible in the treatment of this disease.

Breuil and Dartigneave[13] (1937) after serum therapy and chemotherapy (urotropin, sodium salicylate) failed to act against poliomyelitis in a six-year-old child, reported that transcerebromedullary iodine ionization was followed by rapid improvement.

Maberly[14] (1939) in his book describes four cases of poliomyelitis to which he gave two drachm doses of iodized tincture of guaiacol 6-hourly for three doses and afterwards 8-hourly. All of the cases recovered completely. Maberly remarks that one of the cases was mild enough to have recovered spontaneously, but that the others were severe, showing all the clinical signs of acute poliomyelitis with paralysis, and would otherwise have had an extremely bad prognosis.

Mazzitelli[15] (1939) gave a teaspoonful of iodine-tannic acid syrup twice a day for several days to children in families with cases of

poliomyelitis or in contact with them. None of these children who had preventive therapy developed poliomyelitis in that epidemic or in further ones.

The present writer[16] (1946), in a report on poliomyelitis, suggested the use of iodine in the prevention and treatment of this disease. In a subsequent report[17] (1948), it was pointed out that with a combination of iodine, ascorbic acid and calcium, some poliomyelitis patients improved, in some instances as early as 24 hours after the beginning of the treatment.

The reasons for this combination of therapeutic agents is considered in detail in that report. Briefly stated, the climatic conditions, including heat and humidity, among other factors under which epidemics of poliomyelitis appear, favor the loss of iodine from the body. Iodine is important to muscular tissue. One-half of the total iodine content of the adult human is assigned to muscle iodine.[18] Iodine hastens and strengthens muscle contractions and suppresses the formation of lactic acid by increased oxidation when the muscles are worked.[19] During the summer and fall, the secretion of the thyroid is lowest. The body, thus subjected to a toxin, is able to detoxicate it if the thyroid is functioning normally in order to maintain tissue enzyme systems, particularly those concerned with cell oxidations.

There is a loss of calcium in conditions in which the thyroid is rendered overactive by a toxin. Furthermore, in animals deprived of calcium, paralysis develops. Thus calcium should presumably be available to compensate for that which is lost or rendered unavailable. Cascio[20] (1948) has found that there is a hyperguanidinemia in the majority of cases of poliomyelitis. Calcium has been shown to protect the organism against the numerous pathological manifestations of guanidine intoxication. Saunders[21] (1936) states: "The most efficient management of guanidine intoxication is to combine calcium therapy with other supportive measures, such as forcing fluids and the administration of glucose and an alkalinizing salt for the adjustment of acid-base balance. The activity of the nervous system gradually becomes more normal and respiration improves, indicating increased activity of the respiratory center. There is an increase in blood sugar and a decrease in lactic acid indicating a more normal metabolism. These in turn tend to relieve the acidosis."

Ascorbic acid is a detoxicant and antigoitrogen; it increases thyroid tissue respiration; plays an important role in the metabolism of the nervous system; and protects against liver damage. Ascorbic acid is intimately associated with calcium in metabolic processes in the body.

Lawson[22] (1948) employed furmethide (furfuryltrimethylammonium iodide) for the paralysis of the bladder from poliomyelitis. Excellent results were obtained in 21 (70 per cent) of the 30 patients treated, with almost immediate emptying of the bladder. In those who did not respond so well to the drug, nevertheless, the need for catheterization was decreased by its use.

Ward and associates at New York University[23] (1948) made some interesting observations regarding the use of iodine in experimental poliomyelitis. Working with mice, in a search for a chemical that might reduce the amount of poliomyelitis virus in the stools of victims and carriers, they found that iodine in oil caused a definite reduction in the amount of virus excreted by infected mice treated with this chemical substance.

The Mexican press,[24-27] during July 1948, carried stories of the successful use of iodine in acute, subacute and chronic poliomyelitis by Mexican scientists. The drugs employed were iriodine and radiodine. As far as known to the present writer, there are at this time no reports in scientific journals regarding this work.

IODINE THERAPY IN HERPES ZOSTER

Head and Campbell[28] (1900) described herpes zoster as "acute posterior poliomyelitis." In this disease the anterior horn cells have not infrequently been involved, and paralytic manifestations and atrophy have been observed.

It has been noted by a number of writers that epidemics of herpes zoster (acute posterior poliomyelitis) occur. The frequency of the disease during epidemics of acute anterior poliomyelitis has been observed. In fact, Garrow[29] (1911) was so impressed by this observation that he prepared an article entitled, "Are Polio and Herpes Zoster the Same Disease?" Several writers have reported the simultaneous occurrence of acute anterior and acute posterior poliomyelitis.

Ruggles[30] (1931) reported that intravenous sodium iodide had apparent specific effects in fifteen cases of herpes zoster. He gave

a 20 cc. ampule containing 2 gm. of sodium iodide on the first, second, fourth and seventh days. Two patients received only two injections; four only three. All the cases cleared up in from ten to seventeen days. Pardo-Castello[31] (1931) tried iodide intravenously in cases of herpes zoster and endorsed the conclusions of Dr. Ruggles. He noted remarkable improvement in his cases within a few hours. Phillips and Morginson[32] (1932) employed sodium iodide in the treatment of herpes zoster and say of it: "Under our direct observation and our recommendation, we have seen sodium iodide give almost phenomenal relief in eleven cases of herpes zoster and one case of herpes simplex."

Beers[33] (1939), in the summer of 1935, had a succession of twelve or more cases of herpes zoster in a very short time. He employed Ruggle's treatment, "with really miraculous results." He gave the iodide every other day and found that never more than four doses were necessary. Hinojosa[34] (1947) also found sodium iodide to be exceptionally effective in the treatment of herpes zoster.

IODINE IN THE TREATMENT OF ENCEPHALITIS AND PARALYSIS IN ANIMALS

The iodine treatment of paralytic manifestations has not only been applied to human paralytic disease, but it has also been employed in similar conditions in animals.

Lewitus[35] (1935), without citing specific examples, states that iodides have been used with surprising results in cases of inflammation or effusions involving the spinal cord or brain, such as meningitis.

A poultryman, W. R. Brinton of Glenrose, Pa.[36] (1931-1932) reported that the leg weakness in his flock of chickens, produced by feeding an excess of wheat, was successfully cured with iodized buttermilk. Later he prevented both leg paralysis and coccidiosis by feeding the iodized buttermilk.

Gray[37] (1940) employed a 10 per cent solution of potassium iodide in distilled water in the treatment of fowl paralysis (lymphomatosis). After the first injection of the iodide the birds became brighter, and after the second injection muscular tone began to be restored. Within a period of four to seven days after the second injection the chickens completely recovered the use of their legs and could walk, run, flutter and perch with ease.

Radeleff[38] (1946) employed iodine in the treatment of equine encephalitis. He points out that previous to the routine use of sodium iodide in cases in his practise, the mortality in the area varied from 40 to 50 per cent. During the time of the trials of sodium iodide, the area mortality was about 40 per cent. In cases treated with iodide, the mortality was less than 10 per cent. Those animals treated with sodium iodide recovered more rapidly and the period of convalescence was much shorter than with other methods.

Radeleff points out that the dosage of sodium iodide can be varied with safety over a fairly wide range. The optimum dose that he employed was 5.0 Gm. (75 gr.) per 100 pounds of weight. It was repeated, if necessary, in three days without ill effect.

There were only three fatalities (7 per cent) out of the 43 cases treated with sodium iodide. Repetition of the initial dose of the drug was required in only 20 per cent of the animals. There were no residuals in any of the treated cases.

An editorial in Veterinary Medicine[39] (1942) entitled, "Iodine in the Treatment of Range Paralysis" comments on Gray's experiments and adds: "The recovery and subsequent fertility of apparently incurable cases of fowl paralysis has been experienced also by farmers who have applied the treatment in the field." Bakker[40] (1941), in an article entitled "Potassium Iodide as a Cure for Fowl Paralysis," points out that he employed Gray's iodide treatment for this disease with striking results.

The Iodine Educational Bureau (London)[41] tested Gray's method, in 1947, on two poultry farms near Oxford where cases of fowl paralysis had been reported. Seven severely affected birds were withdrawn from the flock—three from one flock and four from the other—and treated with 5 cc. of a 10 per cent solution of potassium iodide as Gray directs. The remaining birds in each flock (in none of which had fowl paralysis actually developed) were divided into two groups, one of which was given preventive injections of potassium iodide and the other left untreated as control.

"The results were very striking. The severe cases at once responded to the treatment and recovered as Gray described. Those birds showed various stages of paralysis from complete inability to move, except by pushing the recumbent body sidewise along

the ground with one sound leg, to the ataxic stilted gait of the less extensively paralyzed. . . . Not one of the birds in the two groups which were given preventive treatment developed the disease; but in the two untreated control groups a total of six birds (three in each group) succumbed or were killed. The general health, appearance and vigor of the treated birds greatly improved; laying was more prolific, appetite increased and they ranged well for food."

Edward[42] (1948) made interesting observations regarding the use of iodine in the prophylaxis of equine encephalitis. He points out that 1939-41 were encephalomyelitis years. "My herd of horses seemed to have an immunity," he says, "for not until 1941 did the disease hit. Then a six-month-old colt went down with it and to our surprise recovered with a minimum of care and no medication. The same summer a survey of the area proved no cases of encephalomyelitis in horses on routine iodine therapy."

It is significant to note that a number of workers, including von Economo,[43] have employed iodine in the treatment of human encephalitis with favorable results.

In an editorial in the Journal of the American Veterinary Association[44] the reports on the prophylaxis and treatment of equine encephalitis with iodine by Radeleff and Edward are reviewed. It is pointed out that Holtman[45] (1946) had made known his belief that there may be a relationship between the level of the thyroid secretion and susceptibility to human poliomyelitis and encephalitis, due to the fact that these diseases occur in warm weather when natural secretions of the thyroid are the lowest. The editorial states: "Added up, these observations, suggest that Radeleff may have put his finger on something profound. Research men might well give serious thought to the thyroid and its iodine content in relation to the incidence of this disease."

COMMENT

The endless search for a specific drug for the treatment of human poliomyelitis has not been encouraging. Any therapeutic agent that has been shown to produce results in cases of poliomyelitis and other paralytic diseases is worthy of consideration. Iodine, known for over a century, is nothing more or less than a mineral constituent of the body. Moreover, it is an essential ele-

ment of mineral metabolism. Landon-Brown[46] (1943) in his "Physiological Principles of Treatment" remarks: "Nothing could be more reasonable than to use intelligently in disease those very drugs by which the body is enabled to do its work in health." Iodine, in addition to being a normal metabolic constituent of the body, is a virucide. Further, according to the United States Dispensatory[47] it is deposited in the tissues, especially in nervous tissue, when combined with a fatty acid, where it slowly liberates its iodine to exert the therapeutic effect of the iodides.

Since Manson's report in 1825 of the use of iodine in the treatment of human paralytic disease, other reports have continued to appear which have also indicated encouraging results in the treatment of poliomyelitis. Although iodine, like most other therapeutic agents employed in medicine, may not be effective in all cases, it still is, when given a fair and unprejudiced trial in a sufficient number of cases, as Manson said 123 years ago "greatly superior to any remedy we possess, in the different forms of palsy." A statement such as this one cannot be applied to any therapeutic agent that has been thus far employed in the treatment of poliomyelitis.

The therapeutic value of iodine in Grave's disease is well-known. That the thyroid gland is involved in cases of poliomyelitis has been mentioned by several investigators. Stern[48] (1911) found that a considerable number of cases of poliomyelitis showed some symptoms of Basedow's disease, i.e., goiter, tachycardia, tremor, nervousness and the like. In fact, he states that if a patient with poliomyelitis or encephalitis does not show some "Basedowoid" symptoms, the prognosis is less favorable.

Waldenström[49] (1945) reviewed and described many neurologic phenomena of Grave's disease, encephalopathies, asthenias, apathies, athetotic and choreiform movements, in all of which he suspected iodine want may play a role. Means[50] (1948) points out that the muscular symptoms in Grave's disease vary from mild myasthenias to profound muscular weakness and atrophy.

SUMMARY

1. Manson (1825) was the first to employ iodine in the treatment of human paralytic disease. His results were gratifying even in cases where the disease had existed for some time.

2. The use of iodine in human poliomyelitis by a number of workers, including the present writer, is reported.

The writer wishes to express his appreciation to his wife, Alice Gilmore Scobey, R.N., for her helpful suggestions and cooperation in the preparation of this paper.

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A Fifteenth Century Pediatrician

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In the course of my studies on the reactions of newborn children during the adaption period to the extrauterine life, I found an interesting note in Mayerhofer's paper on *Allergie beim Neugeborenen*. He mentions that a physician, Bartholomaeus Metlinger, at the end of the fifteenth century, had the idea that some rashes in newborn babies were the sign of the child's attempt to clean himself of the bad blood transmitted from the mother. The idea of a reaction by the newborn to maternal substances was expressed 500 years before the discovery of transplacental immunization and blood group incompatibility.

I became interested in the man, Metlinger, and his work. I am convinced this clever physician, who was the first to publish an original paper based on his own experience, should be remembered by the pediatricians of our time. A retrospective view from the high of our present knowledge may be useful and interesting.

Here a quotation from Goethe's Faust I.**

> . . . Es ist ein gross Ergetzen
> Sich in den Geist der Zeiten zu versetzen;
> Zu schauen, wie vor uns ein weiser Mann gedacht
> Und wie wir's dann so herrlich weit gebracht.

Little is known about Metlinger's life. He was born in Augsburg, Bavaria, where his father, Peter Metlinger, was a physician —the exact year is unknown. He studied medicine in a number of European universities, did post-graduate work in Ingolstadt, Bavaria, and settled down to practice medicine in his native Augsburg. Judging from the tax records he was a busy and prosperous practitioner. He died in 1491 or 1492—and there we have the bare facts of his life.

But his little treatise "Ein Regimen der jungen Kinder" (Regi-

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**. . . 'Tis pleasant to transport
Ourselves into the spirit of ages past
To see what long ago some sage has thought
And what great climax we've attained at last.

men for Young Children) reveals a good deal more about the sort of man and physician he was.

We have to remember that the basis of medical education in the medieval age was to memorize and follow strictly the doctrines of the old Greek and Arabian physicians. The medical treatises and textbooks were merely compilations or anthologies of these ancient writings.

Metlinger's little book was a milestone in the development of medical writing. It was a new type. It offered advice—not to scholars and physicians—but to parents for the care and treatment of infants. It was based on the author's own experience and, furthermore, written in the language of his day and land—in Old German.

Metlinger was not one of the great physicians of the past and his contribution to our knowledge is very slight. But his booklet —the only paper he published—reveals a warm-hearted, experienced physician and illustrates the low, low level of medicine in the dark period of the Medieval Ages.

What might have induced Metlinger, who was just a simple practitioner and not at all a scholar, to write the Regimen Karl Sudhoff offers a plausible suggestion. In 1472, Pablo Bagellardi, a physician and professor of medicine in Padua, had published "Opusculum de ergritudinibus infantium", a paper on children's diseases. This was a compilation of the maxims of the Greek and Arabian teachers and was written in Latin. It was an immediate success and was reprinted repeatedly and translated into a number of languages. This may have influenced Metlinger to write a similar booklet. Whether it was Metlinger's idea to write this book or whether it was Guenther Zainer, a book printer in Augsburg, who asked Dr. Metlinger to undertake this task, we do not know, but, nevertheless, author and publisher met, and on Tuesday, December 7, 1472, the "Regimen der jungen Kinder" came off the press and immediately became a best-seller. In the following years it was reprinted and translated into French, Dutch and Latin.

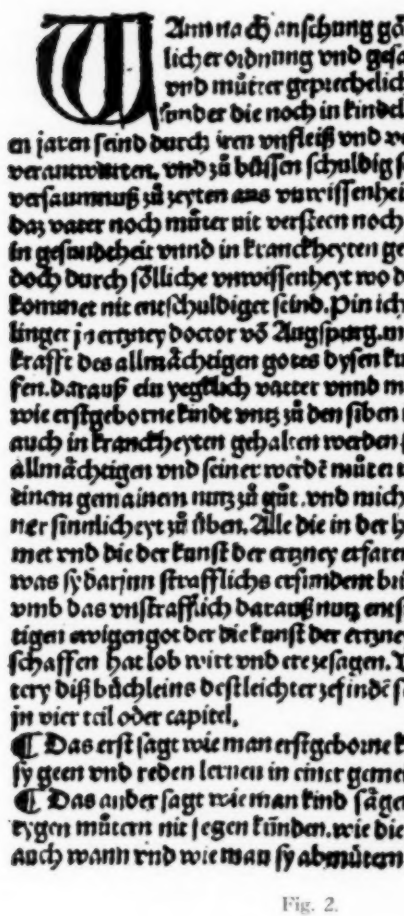
It is not the intention of this paper to translate Metlinger's booklet—there are good translations by L. Ungar (German) and J. Ruhrah (English); there is also no need for a discussion from the historical point, for this has been done by K. Sudhoff and others. I do want to point out, however, the peculiar mixture in

Metlinger's comment. As long as he refers to things he really knows, based on keen observation, he writes sensibly and his advice is good and clever. But as soon as he starts speculating

Fig. 1.

about manifestations or symptoms he does not understand, he becomes absurd and offers the mystic and superstitious ideas of the Medieval.

The title page shows a complete picture of fifteenth century middle class family life. The father is doing accounts, the mother is spinning and at the same time rocking the cradle, an elder daugh-



WAnn nach anschung gōtlicher vnd mensch-
licher ordnung vnd gesatzt. ein yeglich vater
vnd mūter geprechelicheit so iren kinden be-
sonder die noch in kindelichem alter vnder sib
en jaren sind durch iren vnfleiß vnd versaumnuß zůstet yā
verantwurten, vnd zů büssen schuldig sind. vnd aber sōlich
versaumnuß zů zeyten aus vnwissenheit beschehen mag. also
daz vater noch mūter nit verstēn noch erkēnen wie die kind
in gesundheit vnnd in kranckheyten gehalten werden sōllen.
doch durch sōlliche vnwissenheyt wo die durch vnfleiß dar-
komen nit entschuldiget sind. Pin ich Bartholomeus met
linger jn ertzney doctor vō Augspurg. mermals bewegt durch
krafft des allmächtigen gotes dysen kurtzē auszug zů begreif
fen. darauß ein yeglich vatter vnnd mūter verstēn mügen.
wie erstgeborne kinde vntz zů den sibē iaren jn gesundheyt
auch in kranckheyten gehalten werden sōllen. Zů lob got dem
allmächtigen vnd seiner werdē mūter marie der lunckfrawē
einem gemainen nutz zů gůt. vnd mich selbs in erhebung eig
ner sinnlicheyt zů übē. Alle die in der hennd dyß büchlein kō
met vnd die der kunst der ertzney erfaren sind mit fleiß pittēt
was sy darjnn strafflichs erfindent brüderlich zestraffen vñ
vmb das vnstrafflich darauß nutz entstēn mag dē allmächti
gen ewigen got der die kunst der ertzneye vnnd alle ding ge-
schaffen hat lob wirt vnd ere zesagen. Vnd vmb das die ma-
tery diß büchleins destleichter zefindē sey hab ich es geteylet
jn vier teil oder capitel.

¶ Das erst sagt wie man erstgeborne kind halten sol biß daz
sy geen vnd reden lernen in einer gemein

¶ Das ander sagt wie man kind sāgen sōll. vnd wann sy ir
tygen mūtern nit segen kūnden. wie die sigam gestalt sein sol
Auch wann vnd wie man sy abmūtern sol

A ij

Fig. 2.

ter, still unwed as witnessed by her braids, is also spinning; a young child is looking at a book, and the dog is peacefully asleep. (Fig. 1)

The preface is very interesting. Metlinger introduces himself as a doctor and declares that—with the help of God Almighty—he will advise parents how to care for their children in health and disease—from birth up to seven years. He then continues: "All to whom this booklet comes to hand and who are experienced in the art of medicine I earnestly beg, if they find anything blameworthy in it, to criticize it in a brotherly way, so that the blameless part can be used and Almighty God, who has created the art of medicine, may be praised. . . ." (Fig. 2) Might not this be a good invocation for the modern book reviewer?

The preface ends "and in order that the material of this booket could be easily found, I divided it in four parts or chapters." "The first tells how to care for newborn children till they have learnt to walk and talk."

The chapter starts with detailed directions of things to be done immediately after birth. The midwife must cover her finger with honey and put it into the mouth of the newborn infant in order to dissolve adhesions. This dangerous practice continued for centuries after Metlinger's day. Next the infant's body was to be sprinkled with salt, or better still, with salt mixed with powdered herbs. In this he differed from Avicenna, who thought that salt bites and preferred an ointment with acorn oil. The advice for the care of the navel is excellent, evidently based on good observation; some are peculiar, for example, the application of pulverized calf's hoof.

A daily bath—cool for the male child, warmer for the daughter—is advised for the first six months. The child should sleep with the head slightly raised on a pillow, for "much harm can come from the bad habit of old women to have the children sleep flat; running ears and misshaped heads."

The concluding remarks of this chapter prove Metlinger's excellent observation. He states: "Healthy children behave well and do not complain. If babies cry and whine, there is unhealthiness in them, and one must look for the cause and remove it." Then he enumerates the many causes: "pain, wetness, urge to defecate, too tight clothing, the feeling of being too cold or too warm, and, finally, the desire to be picked up because it does not want to be alone." To comfort a crying baby, Metlinger recommends: 1. Give the infant the breast; in most cases this will satisfy the child,

2. Sing with a soft voice. 3. Rock the cradle gently. In the five hundred years that have passed, these basic methods, arising from the motherly instinct, have not changed.

Chapter two deals with breast feeding, either by the mother or by a wet nurse. Artificial feeding was practically unknown in the fifteenth century. This part of Metlinger's booklet is excellently written. He describes in detail the requirements of a nursing woman, her diet and how to ascertain the best quality of her milk.

Metlinger follows the ancient physicians in believing that the mother should not nurse her infant during the first two postnatal weeks because her milk during this time is not good for the child. During this period, therefore, the baby should be nourished by a woman, who had given birth some weeks earlier. The mother's breast should be sucked by a "young wolf." Both Ungar and Ruhrah write wolf without hesitation. It seems unlikely that a sufficient number of these animals roamed the streets of Augsburg in the fifteenth century or that Metlinger had in mind the amorous young male of our day. In all likelihood Metlinger's"wolf" meant puppy. If the mother wants to nurse her child immediately after birth, a bit of honey should be put into the babies mouth before sucking, to prevent harm from the milk.

Then follow extensive prescriptions for the diet of nursing women; it varies according to the quality of the milk, whether it is too thick or too thin. The advice for a nursing woman with fat milk: eat less, avoid beer, fat cheese and pastries, and work more—quite similar to a modern reducing diet. There are many directions for preparing foods and drinks with herbs and spices, etc., in order to influence the quality of the milk. These are based on the then current ideas and superstitions about the effect of herbs or animal organs. But, certainly, when he advises a mother with an insufficient milk production to eat the udder of a goat or sheep who had given birth and suckled her young, he is the predecessor of organ therapy.

The qualities of a wet nurse are discussed in full detail; the physical condition, the quality of her milk and her character. "She should have good and praise-worthy habits, not be easily frightened or worried. She must not be small-minded or prone to anger (was this based on experience in his own household?). She must behave correctly, because whatever undesirable habits the nurse has, will

be transmitted to the infant, and, finally, she must take care not to become pregnant.

Metlinger advises that the child should be weaned gradually, and he favors the use of a goat-milk formula during this period. Metlinger concludes this chapter with a very nice personal remark: " . . . if I have prolonged in my writing what I had to say concerning these matters, may no one bear me ill will. . . . For the health of the child is bound up with the welfare of the nursing women."

Chapter three is, of course, the most interesting for the pediatrician. It reveals the mystic ideas of the Middle Ages about the origin of diseases. But Metlinger does not repeat slavishly the ancient Greek and Arabian doctrines. Of course he quotes Hippocrates, Galen, Avicenna and others, when he is startled by a symptom or sign which he does not know how to explain. But here and there one comes across an idea obviously based on his personal observation and experience. Metlinger discusses twenty-five affections, afflicting children during early life and the majority of his observations concern breast-fed infants. This explains his astonishing statement: "If the infant is ill, the nursing woman should behave as if she herself had the disease . . . and if the infant refuses to take the medicament, she must swallow it herself." Perhaps that explains the good therapeutic results of his prescriptions. He is convinced that most of the diseases in infants arise from "bad" (incompatible) milk. Therefore, the nursing woman must be treated before starting any treatment of the infant. If she is plethoric, blood-letting is indicated; if she is pale, laxatives and tonics."

Metlinger is dissatisfied with the old classification, which divided the childbirth diseases into those (1) before the teeth are cut; (2) during teeth cutting and (3) after teeth cutting. He prefers the generally accepted classification of disease "De capite ad pedes," from the head to the feet. Therefore, he starts describing affections of the head, face, neck, etc., and gradually proceeds downwards.

In describing each disease he starts with a short definition and sometimes mentions a few symptoms; these are usually clearly given because the old master tells what he has observed. But when he starts to discuss etiology the result is very often fantastic and mystic speculations. The same is true for his directions for treatment. Recommendations of abstruse mixtures and concoctions of

herbs, spices, extractions of animal organs, are based on the contemporary belief about the effectiveness of these preparations. But some therapeutic recommendations are good and a few are still in use after 500 years.

I do not intend to discuss all the twenty-five diseases Metlinger has described, but I do want to point out a few of them which will illustrate the characteristic mixture of good observation and common sense with fantastic nonsense and superstition.

I. *Verriss*, that means eczema of the head and face. It is supposed to originate by an excess of blood and humidity oozing from within the head to the surface. Local treatment: cut the hairs, cover with wet dressing till the crusts come off. If there is oozing of a yellow honey-like fluid, use a mercury or sulfur ointment. Now, 500 years later, practically the identical treatment is in use.

II. *Unnatural Largeness of the Head.* Understandably, the grotesque malformation of a hydrocephalic head aroused fantastic ideas and gave rise to mystic speculations. Metlinger states correctly that the enlargement is caused by an accumulation of fluid within the head, and then goes on to say: ". . . that the enlargement generally appears on the seventh day of life, the time of great changes in the child. These children, therefore, are called "Wechselkinder," literally changed children. We do not know what Metlinger meant, when naming the hydrocephalic babies Wechselkinder. For centuries "changing" was the name for a malformed or dwarfish individual, supposed to be placed by witches for the normal one, they had stolen. And still later the term "Wechselbalg" came to be used as a word of opprobrium for an ugly, nasty child. Metlinger continues, "all hereditary diseases are postponed until the age, when conditions for their appearance are suitable.*

"As long as the fetus is in his mother's body, the heat (internal warmth?) of the mother and the delicacy of the fetal brain-covers destroy the vapors(?). After delivery this no longer takes place, the vapors ascend to the head and condense to water."**

Metlinger offers a great number of directions for treatment, diet, lotions for the bath, lily or majoram water as a drink for both

*Evidently Metlinger had recognized that the first week of life is characterized by the appearance of a great variety of peculiar symptoms; the so-called biologic reactions, considered by Mayerhofer and Lehndorff as manifestations of allergy of the newborn to maternal substances (see disease xxv).

**Centuries later the "detoxifying activity of the placenta was vividly discussed."

the baby and the nursing women and, among others, a piece of cotton with drench, a mixture of wolf's gall, wolf's brain and myrrha and place it in the nostrils of the child.

III. The third disease in Metlinger's enumeration is called "*Durstig*," i.e., "thirsty," describing a condition which might be meningitis or a severe dehydration.

IV. The fourth disease is named "*Wacking, sleeplessness*". "Insufficient sleep can start many affections, which would disappear during sleep. Heavy vapors in the head may arise from a strong milk." Some prescriptions may be quoted. Mix the milk of a woman that has suckled a daughter with the white of an egg and the juice of lettuce and instill a few drops into the child's nostrils or use an ointment prepared from white poppyseed and henhamp and rub it to the temples.

V. *Vergicht.* Very interesting are Metlinger's ideas about convulsions, the falling disease. Convulsions immediately after birth are caused by an unmoral conduct of the pregnant mother ("who leaves herself open for desire either good or bad"). If convulsions are combined with imbecility, nothing can be done; it comes from the influence of the stars. Convulsions in elder infants are caused by bad milk, irregular feeding, teething, fright, etc. The advice is as follows: First protect your child with the help of God. Then the nursing woman must avoid apples and—sin, finally a great number of preparations from many herbs, spices and animal organs are listed, and, in accordance with the temporary belief, Metlinger suggests to "put a peony root or an emerald or another green gem on a chain around the baby's neck".

VI. *Paralysis.*

VII. *Discharge from the Ears.* The suggestions for treatment are quite modern; clean and dry the ear, put in an alcoholic (wine) solution of alum or myrrh.

VIII. *Eye Affections.*

IX. *Squinting.* To correct a squint, cover the child's head with a cap. Let the child look with the squinting eye through a hole in the cap at a mirror until he falls asleep.

X. *Teething.* Here we find again the mixture of very good observation and rank superstitution. There is considerable discussion of the influence of the seasons and the predisposing role of teething in the development of various diseases. We should

remember that such discussions were continued for many centuries and Metlinger's advice to let a teething baby chew on a violet root was followed by generations of mothers and midwives. Another suggestion is: rub the jaws of the child with a lotion prepared from hare's brain, chicken fat and a bitch's milk. It is interesting to note that Metlinger never gives a reason for such therapeutic recommendations.

XI. *Swelling of the Jawbone and Around the Neck.*

XII. *Blisters in the Mouth.* Metlinger describes white blisters (thrush), yellowish ones (aphthae) and black ones, which he says are very dangerous; apparently he has observed noma.

XIII. *Cough and Shortness of Breath.* These conditions develop when the tongue does not adequately protect the respiratory tract from cold air. Some prescriptions are still used, e.g., milk of almond and tisanes with licorice, taraganth and fenchel.

XIV. *Indigestion and Hiccup.* Usually caused by overfeeding.

XV. *Jaundice* is caused by an inadequate—too fat or too coarse —milk, which obstructs the ways in the liver and gall bladder.

XVI. *Ruhr.* This is shortly discussed. Metfinger recommends drastic reduction of food for the nursing women; she should drink skimmed goat's milk.

XVII. *Constipation.* As in every disease bad milk is the etiologic factor; besides a well considered diet, the nursing woman should take a laxative and the baby may get a suppository prepared from salted lard.

XVIII. *Prolapsus Ani.*

XIX. *Worms and Abdominal Pains.* Here again is an example of how some peculiar ideas are kept alive in folklore for centuries. Chewing during sleep and itching around the nostrils in daytime are still believed as signs of worm infestation by many mothers.

XX. *Hernia Inguinalis and Umbilicalis.*

XXI. *Stones in the Urinary Bladder.* These develop when the mother eats too much cheese or blackberries or elderberries. If a tisane of green walnuts, thistle syrup and allum does not work have the child operated on.

XXII. *Furuncles, Abscesses and Ulcers.*

XXIII. *Fevers.* If children show more heat than they should have or alternate heat and cold, then they suffer from fever.

XXIV. *Erysipelas.* It is the heated blood driven out from the

inside of the body to the surface; one should take care that the erysipelas is not driven into the inner organs, the vital parts.

XXV. The last, longest and most interesting discussion of diseases deals with *"Durchschlechten und plattern"*, that means with skin eruptions and smallpox. It starts as follows: "Skin eruptions and smallpox come from an inflammation of the blood, which drives out the impurities which the fetus has received from the "verheptem", blood of his mother. Here some difficulty arises. We do not know what Metlinger had in mind. Verhapt is translated by Ruhrah as "crude", by Ungar—it might mean verstockt, coagulated; Mayerhofer just says "bad" and in Sudhoff's monograph as well as in Grimm's dictionary it is translated "verhalten", i.e., retained. Whatever Metlinger had in mind, we cannot know. But the following sentence gives some idea: "It should be known that the fetus is nourished from the most delicate and purest blood of the mother . . . nevertheless the child's blood receives a mixture in his blood, because the verhepte blood lies all about it. . . . Therefore a child may be cleansed at least once before the end of his life by skin eruptions. . . ." The important point in Metlinger's discussion on rashes in the infant is, that he assumes, that the child's blood contains maternal substances, transmitted via placenta or during labor—where there is "verheptes" blood lying around, and that the child has to get rid of these incompatible maternal substances. This idea of placental transmission of maternal proteins, which may under certain conditions sensitize the fetus and produce rashes as a manifestation of an allergic condition of the newborn, was pronounced five hundred years before the discovery of the mutual immunization between mother and child. The idea that the newborn has to clean himself from the "bad" blood transmitted from the mother is believed in folklore from ancient time to the present. Mayerhofer tells us, that in Croatia the farmers' women are convinced that the newborn has to clean himself after birth by exanthemas.

The remainder of the discussion in this chapter is a rather confused affair, as evidently eruptions of all kinds are mixed up. "The skin eruptions may appear earlier or later in life, according as the nature is inclined to drive out the superfluous moisture . . . and there is, of course, the influence of the stars".

The last chapter of Dr. Metlinger's little book is a charming

proof of the warm-hearted, clever and experienced physician and father. He discusses how children should be treated and educated when they have learned to walk and to talk. What Metlinger has to say about teaching the child obedience, the child's need of play, and the danger of severe punishment is not in the least ancient. Here in this chapter he gives a number of case histories. One of those may be quoted; "There was a man who noticed his son's desire for his stepmother, so he led the boy to another woman, thereby avoiding great evil".

Curiously enough, while Metlinger's counsels show common sense and experience, the reasons he gives for his suggestions are often absurd. For example: a child should not be showered with cold water. By doing so, "internal diseases are invited and external diseases are kept from erupting". A child should not drink wine before puberty. Very well, but why? "Wine inflames and over-moistens the head, makes it watery, which causes various diseases and overexcitement of the spirit and disposition to anger".

"And with this, the fourth chapter and the little book ends".

ACKNOWLEDGEMENT. I want to express my grateful appreciation to Dr. Kurt Proskauer and the Rare Book Department of the Academy of Medicine, New York.

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INTERESTING CLINICAL SYNDROME: MELANODERMA CIRRHOSIS OF THE LIVER AND DIABETES MELLITUS. (Hospital, Rio de Janeiro, 39: 275, Feb. 1950). The case described by the authors is rare. The patient, a girl 14 years old, had from the age of 8 a progressive disease characterized by pigmentation of the skin, hepatic cirrhosis with splenomegalia and diabetes mellitus simulating hematochromatosis. Neither biopsy of the skin nor post-mortem examination revealed existence of hemosiderin. The authors concluded that the case was one of cirrhosis of the liver in association with diabetes mellitus and melanoderma of unknown origin. The suprarenal cortex was found to be normal by necropsy.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

THE PAROXYSMS OF WHOOPING-COUGH TREATED BY PULLING THE LOWER JAW DOWNWARDS AND FORWARDS (NAEGELI)*

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In the third edition of his "Therapeutics of Infancy and Childhood" Jacobi[1] says: "The mortality from whooping-cough in New York City is as great as that from typhoid fever. Twenty-five per cent of all the cases under a year terminate fatally, 5 per cent of all those between the first and fifth years, and 1 per cent of all those occurring after the fifth. Its direct mortality, however, is not the only danger, for not infrequently chronic laryngitis, pneumonia, emphysema, dilatation of the bronchi and the results of hemorrhages which occur during the attacks (convulsions, paralysis, either general or local, blindness) impair the health of the patient for many years or a lifetime. Thus the tendency to allow whooping-cough to run its full course on the plea that it is a self-limited disease or that every child must have whooping-cough is not justified." Such statements carry with them a forcible argument for exerting renewed efforts to mitigate or cure this obstinate and dreaded affection, and to guide our cases to a favorable issue.

In the treatment of whooping-cough two facts have been definitely established: first, that all measures to be efficacious must be directed toward diminishing the number and severity of the paroxysms, and, second, that the success of medicinal treatment thus far has been in inverse proportion to the remedies recommended for the cure of the disease. The drug treatment of pertussis, despite the various preparations recently introduced, has been so unsuccessful that any new measure having for its object

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the alleviation of the patient's sufferings must certainly be considered as worthy of attention. So many and varied have been the drugs recommended for this disease, that it would be an easier task by far to mention those that have not been tried. To the credit of the profession be it said, however, that the vast accumulation of literature on the subject, is but another expression of its tireless search for remedies to alleviate or cure suffering.

It is not my purpose to review or pass upon the merits of all the drugs and procedures that have been recommended for this affection—antispasmodics, narcotics, nervines, anesthetics, astringents, inhalations, local applications, intubation, tracheotomy, vaccination, formalin, diphtheritic serum, counter irritation over the pneumogastric, compressed air, carbonic acid gas per rectum, suggestive therapy, ozone, pertussis serum (Leuriaux[2])—nor to discuss the various theories of its causation—microbic, neurotic, specific catarrh of the respiratory apparatus, general infectious disease, irritation of the vagus by enlarged bronchial and tracheal glands (Guéneau De Mussy)—but rather to present for consideration, and I hope for trial, a method which I have applied in a series of cases and one which I believe should be more universally known and practised.

Some two years ago, in reading one of the clinical lectures[3] delivered at the New York Post-Graduate Medical School by Dr. Augustus Caillé, I met with the statement that manipulation of the lower jaw as practised during the administration of an anesthetic would overcome the asphyxia of a whooping-cough paroxysm; or, to use his own words: "The attack of spasmodic cough which you notice is now coming on can be checked by pressing forward the lower jaw as you would in a narcotized patient who was not breathing properly. In some children whooping-cough attacks are so severe that they will end in convulsions and it is well to know in what manner such an attack can be easily stopped." Though a mere statement of fact, without any attempt at an explanation of its effect, I considered the method deserving of a trial, in view of the absence of any known specific for the disease, and because of the usual lack of success in treating it. At that time, the clinical material at my disposal was unusually large and enabled me to give the method a thorough trial; that is, as thorough as is possible with dispensary patients. I desire to state

at this point, that when I began my observations I had no knowledge of the article by Naegeli to which I will refer later.

Accordingly, all cases of whooping-cough presenting themselves at the dispensary from June 1901, to the present date, were subjected to this treatment at the time of their visit and the following results were obtained: In all, 96 cases were recorded, ranging in age from three months to eight years; no selection of cases was made, the children being taken as they came; all grades of severity and all stages were observed, those with and those without a whoop. In the latter class (5 in all) the diagnosis was based upon the prevalence of the disease in the immediate vicinity, the history of exposure, the characteristic expulsive expiratory cough, the vomiting, congestion of the face, edema of the lower lids and the usual absence of bronchitis. Of these, I can report but nine failures (about 9⅓ per cent), that is, nine in which the method had absolutely no effect on the paroxysm at the time of the child's visit to the dispensary. Two of the failures occurred in the cases without a whoop. In the remainder, there never was a time when at one visit or the other I could not control the paroxysm and the oncoming whoop by pulling the lower jaw downwards and forwards. It may be, that even in the failures success would have been attained at some time or other could the procedure have been carried out regularly at home. In infants and young children the method seemed less efficacious than in older ones; they were more easily frightened by the maneuvre, and as they could not be assured that the method was painless, their crying rather increased the severity of the paroxysm or brought about another. That crying, emotion, changes in temperature, swallowing, and irritation of the throat precipitate an attack is well known. In some young children, however, it acted remarkably well. It would be highly desirable if the effect at the different ages was reverse, inasmuch as the younger the child the greater is the danger of profound asphyxia and convulsions. In some instances, when the lower jaw was pulled forwards at the beginning of the attack, the paroxysm ceased as if by magic and no whoop occurred. It may be questioned how it is known that in this set of cases a whoop would have occurred. As a control experiment, after arresting the expiratory spasm, another paroxysm would be brought about by suprasternal pressure or an examina-

tion of the throat, the patient would be permitted to whoop once or twice and then at the end of the second or third expiratory spasm, that is, just before the expected whoop, the lower jaw would be pulled downwards and forwards and no whoop would occur. In the series, 2 cases of epistaxis were noted in which during the paroxysm blood would literally pour from the nose; in these, the method acted well and the bleeding was controlled. One boy of eight years had a severe subconjunctival hemorrhage which increased daily; in this instance pulling the lower jaw downwards and forwards stopped the paroxysms and with them the danger of further hemorrhage. Many mothers became frightened at the sight of my pulling the jaw, but when they noticed the good effect, their faces assumed an expression of satisfaction and relief. Older children were also alarmed at first, but later submitted willingly; in fact, some of them hastened to me for relief at the onset of the attack. In most of the cases, and more particularly when the paroxysms were severe and frequent, the method was demonstrated to the mother or attendant, with instructions to adopt it in general, and always for the night attacks. Many returned to state that it proved successful.

O. Naegeli,[4] to whom is due the credit of first advocating this method of treatment for the paroxysms of pertussis, after stating in his article of July 1889, that to cure without medicine is the ideal therapy and that physicians have become sceptical as to a new specific for the disease, expresses the hope that in recommending a simple maneuvre to control the asphyxia of a whooping-cough paroxysm, the profession will give him a favorable hearing. Unfortunately, his contribution has fallen by the wayside, for with few exceptions I can find no reference to it in medical literature. The mere fact that the standard works and writings of Henoch, Jacobi, Baginsky, Monti, Filatow, Marfan, Koplik, Holt, Genser, Seitz, J. Lewis Smith, Ashby and Wright, Eustace Smith, Griffith and Dawson Williams, which refer in extenso to the various measures recommended, contain no mention of this procedure is to my mind a proof that the article has been overlooked rather than that it has been considered unworthy of note. In fact, the very recent contribution on whooping-cough by George Sticker,[5] while quoting a very extensive literature, also fails to mention Naegeli or his method. Whitla,[6] in his Dictionary of Treatment, and Escherich,[7]

in his article on tetany, speak of it in passing. O'Dwyer and Norton,[8] under the heading of mechanical treatment, say: "Naegeli reported that in two children he succeeded more than five hundred times in apparently arresting the spasms of pertussis by pulling the lower jaw downwards and forwards. His experience, however, so far as can be found, has never been confirmed by other observers." H. Neumann[9] remarks that for arresting the attack it has been recommended to pull both cornua of the hyoid bone upwards for sixty to ninety seconds or the lower jaw forwards. Eichorst[10] mentions at the extreme end of his article, "manipulation of the lower jaw during the attack as in chloroform anesthesia" (Naegeli).

Naegeli believes that the whole therapy of pertussis should very properly be directed to the glottis spasm, quoting Niemeyer as saying that "every paroxysm of cough is an irritant to the laryngeal mucous membrane; the more violent they become the more quickly fresh mucus accumulates and the sooner another attack is to be expected. If we can diminish the severity of the attacks of cough, the course of the disease will be shortened." He then adds that *if we could arrest the spasm of the glottis the back bone of the disease would be broken.* In this connection, it is interesting to note the statements of O'Dwyer and Norton,[8] who, preparatory to their recommendation of intubation for relieving the spasm of the glottis in pertussis, say: "Spasm of the glottis is the sole cause of the acute suffering in uncomplicated whooping-cough, and could this element be removed the disease would be reduced to the level of an ordinary bronchial catarrh. The fear that children exhibit on the approach of a paroxysm, when they drop their playthings or other occupation and run to the mother or nurse for relief, is not the dread of the cough or the vomiting that follows, but of the torture that results from prolonged spasm of the glottis. In the adult, this feeling is intensified by the sense of impending death which can never be gotten over no matter how often experienced. It is not the last hour that has come, nor the last minute, but almost the last second. The suffering is not due solely to want of air, because it begins the instant the spasm begins and often when the lungs are well supplied with air; on this point, one of the present writers (O'Dwyer) can speak from personal experience, having had

whooping-cough when over forty years of age, and complete spasm of the glottis from other causes many times. *Spasm of the glottis being not only the sole cause of the acute suffering in pertussis but of most of the dangers as well, the main object of medication is the relief of this symptom.*" In describing an attack of pertussis personally experienced in 1886, Naegeli states that at the beginning of the paroxysm he felt as if a trap door had been lowered upon him and had cut off all the air; inspiration became impossible on account of spasm of the glottis, and frequently no mucus was expectorated after the paroxysm; there was a tonic spasm of all the laryngeal muscles, the entire respiratory muscular apparatus of the neck and the muscles of the face partaking of the attack. At the height of the paroxysm, despite a protruded tongue, a condition simulating trismus occurred. He states that, at the beginning a minimum amount of air could be inspired with the well-known inspiratory crow, while at the acme of the paroxysm the cough was toneless. "Now," says he, "could the rima glottidis be opened again so that the inspiratory current would be sufficient, then the whoop, with its congestion and all its consequences, would disappear, as it were, with one blow." He then proceeds to show that Kappeler in his experiments has proven that the asphyxia of chloroform narcosis bears a great resemblance to that of pertussis, the difference being that in the latter, in addition to the mechanical closure of the upper part of the larynx there is a closure of the glottis due to a spasm of the cricothyroid muscles. Kappeler furthermore states that the most efficacious method for clearing the entrance to the larynx is undoubtedly raising the lower jaw after the manner of Howard and Heiberg, which consists in standing behind the recumbent patient, placing the thumbs on the symphysis of the lower jaw, the flexed index finger behind the ascending rami and pulling forcibly and directly forwards. Prompted by these experiments and results, Naegeli applied the maneuvre to his own children of seven and four years, respectively, who were ill with pertussis, trying it for five weeks, day and night, at least five hundred times in all. His results were brilliant at the first attempts, the cough stopping immediately when the lower jaw was raised. After a thorough application of this method he modified it as follows, according as he grasped the lower jaw from (a) in front or (b) from behind.

(a) When in front of the patient he placed the index and middle fingers on the rami in front of the ear, the thumbs on the chin and with a forcible but gentle pull and pressure he pushed the lower jaw downwards and forwards. If the mouth was opened and the tongue extended he placed the thumb or index fingers in the region of the canines, the remaining fingers on the body of the lower jaw and thus pulled downwards and forwards. Very frequently he placed only the thumb or index finger back of the lower incisors, the remaining fingers of that hand under the chin and then manipulated the lower jaw as before mentioned, keeping the other hand on the forehead for counter-pressure.

(b) When behind the patient, he placed both thumbs against the angle of the jaw, the index fingers on the zygomatic arch, the remaining fingers on the chin and thus pushed downwards and forwards; or the index fingers were placed in the mouth behind the canines and thus aided in the manipulation.

When the lower jaw had been raised the patients were directed to take a deep breath. It is understood that this statement applies only to older children.

With my cases, I have found that a single method practically answers every purpose, and so when in front of the patient I place the flexed index and middle fingers against the angle of the inferior maxilla, both thumbs along side of the nose and against the superior maxilla, and then pull downwards and forwards. If behind the patient, I place the flexed index and middle fingers against the angle of the jaw, the thumbs along its body, the remaining fingers beneath it and thus manipulate by pulling downwards and forwards.

It may be asked, whether this maneuvre or grasp, apart from its effect upon the paroxysm, that is upon the glottis spasm and its resulting asphyxia, has any influence upon the character and course of the disease. With a dispensary clientèle, which believes with the South German peasant that whooping-cough "continues till it stops," my observations were necessarily limited, for the greater part, to the effect on the paroxysms. It would follow as a logical sequence, however, that as the glottis spasm is the main element in the acute suffering, complications and sequelæ of the disease, and that inasmuch as it is controlled by this method, it would be but natural to expect that the disease would be very mate-

rially modified in its severity and duration. In fact Naegeli says that, with this treatment, the disease assumed a milder character, there was no vomiting, bleeding and complications due to increased blood pressure were absent, the course of the disease was shortened and the nights were not disturbed. Some may say that in Naegeli's cases, pertussis existed in the attenuated or abortive form spoken of by Henoch, and hence the good effect upon the course, duration, character and complications of the disease was only apparent and would have occurred irrespective of this or any other method of treatment. Admitting this for argument's sake, it still remains true that the glottis spasm, the main element in the paroxysm, is efficiently and almost instantly overcome in the great majority of cases. It thus appears that this method brings about the objects of treatment formulated by Jacobi, namely, "to relieve the severity and diminish the number of the attacks, to procure quiet nights, to stop the vomiting, to shorten the course of the disease and to prevent detrimental consequences." For mothers, nurses and other attendants, this method of pulling the lower jaw downwards and forwards for the control of the paroxysms is to be highly recommended. *Every spasm cut short or arrested, every whoop prevented, spares the heart, lungs, brain and nervous system from so much wear and tear.*

At the beginning of my observations, I thought that the good of this method could be attributed to the pulling forwards of the tongue which had fallen backwards. Soon, however, it was seen that severe paroxysms took place with the tongue protruded, and these were controlled by the aforementioned maneuvre. Naegeli considers the effect of this manipulation due, firstly, to reflex action, producing thereby a relaxation of the tonic muscular contraction, and secondly, to mechanical action, in that by raising the entire larynx and the hyoid bone, the epiglottis is elevated and the rima glottidis perhaps opened. Whether this is the proper explanation or not, or whether by this means the pneumogastric is stretched (counterirritation) or the trachea elongated, with relief of irritation at the bifurcation, I do not profess to know. Certain it is, however, that by means of the manipulation the paroxysm is overcome immediately or in a few seconds in the vast majority of cases. With Naegeli's children the method was successful every time and vomiting did not take place except when

no one was at hand to manipulate the jaw. The maneuvre may be carried out while the child is asleep, so that any argument that the effect is psychical will not hold. The only contraindication to its use is the presence of food in the mouth or esophagus.

Naegeli states that very frequently spasmodic coughs due to other causes may be controlled by this manipulation, though I am free to confess that my experience in this direction has been rather disappointing. Escherich,[7] in discussing the laryngismus stridulus so commonly associated with tetany, says that Naegeli's maneuvre which arrests the attacks of whooping-cough fails in these instances.

To sum up the results of my experience with Naegeli's maneuvre for overcoming the spasm of the glottis in whooping-cough, I should say:

(1) Pulling the lower jaw downwards and forwards controls the paroxysms of whooping-cough in most instances and most of the time.

(2) The method is usually more successful in older children than in younger ones and infants.

(3) In cases without a whoop the expiratory spasm with its asphyxia is generally overcome, and in those with a whoop the latter is prevented.

(4) As a single therapeutic measure for the control of the paroxysms it deserves a place in the treatment of pertussis and is as successful as any single drug, or even more so.

(5) Mothers, nurses and other attendants should be instructed in its use in order that the oncoming attacks, especially at night, might be arrested.

(6) The manipulation is harmless, painless and easy of application without any of the ill effects of drugs; it offers a maximum good effect with a minimum derangement.

(7) The only contraindication to its application is the presence of food in the mouth or esophagus.

(8) Patients treated in this manner are less likely to suffer from complications and sequelæ, than those treated only medicinally; they emerge from the disease in far better condition, less exhausted and less emaciated because vomiting has been controlled.

(9) It is advisable to try the maneuvre in other spasmodic coughs and laryngeal spasms (laryngismus stridulus, pressure of

enlarged cervical and bronchial glands, influenza, glottis spasm in catarrhal laryngitis), although my experience has seemed to show that it is far less efficacious in these conditions than in whooping-cough.

(10) This method, being directed mainly to the control of the glottis spasm, does not preclude the advisability of supporting and sustaining the patient, guarding his gastrointestinal tract, establishing equilibrium in the nerve centres and affording him every possible hygienic advantage.

(11) It is particularly indicated in instances complicated with diffuse bronchitis, bronchopneumonia, convulsions, epistaxis, subconjunctival or subcutaneous hemorrhage, or sublingual ulceration, and in those children who by virtue of age, the presence of rachitis, scrofula or general debility are predisposed to serious complications and sequelæ.

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MERCURY POISONING AS CAUSE OF ACRODYNIA. (Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam, 95: 378, Feb. 3, 1951). In the 2-year-old boy whose case is reported acrodynia developed as the result of treatment with mild mercurous chloride (calomel). Patch tests proved hypersensitivity to mercury, and the urine contained large amounts of mercury. The symptoms of acrodynia subsided following treatment with dimercaprol (BAL). The author cites several other reports from the literature in which children in whom acrodynia developed following treatment with mercury preparations were effectively treated with dimercaprol.—*Journal A.M.A.*

PEDIATRICS HALF A CENTURY AGO

From time to time the Archives, which was the first Children's Journal in the English language, will reprint contributions by the pioneers of the specialty over fifty years ago. It is believed that our readers will be interested in reviewing such early pediatric thought.

SEPTIC ENDOCARDITIS*

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In the spring of 1905 a boy four years of age entered the Cincinnati Hospital with scarlet fever. He had a bad sore throat, associated with a rather severe cervical adenitis. One week after entering the hospital an endocarditis developed which ran a mild course and was not associated with cardiac distress. He remained in the hospital for sixty-eight days and was discharged in good condition.

At the time of his discharge a mitral systolic murmur persisted but cardiac compensation had apparently been established. Five days after his discharge he was taken acutely ill with a severe ulcerative tonsillitis. This new infection was very soon followed by a septic endocarditis and general symptoms of septicopyemia. In five or six weeks these symptoms gradually subsided and the child for a time slightly improved in health and strength. At this time he contracted measles and this aggravated the endocarditis and led to the development of bronchopneumonia and cancrum oris. The child died one hundred and thirty-seven days after the onset of the scarlet fever attack.

I have been much impressed in the study of this case with its close analogy to two other cases of rapidly fatal endocarditis which I have observed in older children. Both of these cases had apparently recovered, with damaged mitral valves and hypertrophied hearts, from attacks of endocarditis associated with severe ulcerative tonsillitis, but with no arthritis. Months later, after an interval of apparently satisfactory convalescences, they were again taken ill with severe ulcerative tonsillitis, together with

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other members of their respective families, and almost immediately severe malignant endocarditis developed, which within fifteen days caused death. One of these cases suffered severely from arthritis, the other had no joint symptoms. The other members of the two households recovered from tonsillitis without joint or heart symptoms.

From the analysis of these cases I think one is justified in the belief that they belong to a type clinically distinct from the endocarditis of true rheumatism. I believe there is a distinct disease known as acute rheumatism, which does not present the clinical picture of septicopyemia, whose bacteriology is unknown and which very commonly produces a non-septic endocarditis. This rheumatic endocarditis is a manifestation of the rheumatic poison which may precede or follow the arthritis and chorea produced by this same poison. It is not ushered in by ulcerative tonsillitis, by diphtheria, by a scarlatinous sore throat or by other local foci of septic infection. It is not infectious, has no septic symptoms, and is favorably influenced by the alkalies and salicylates which act specifically in true rheumatism, but have no influence on the septicopyemic form of arthritis which is associated with septic endocarditis.

The bacteriology of septic endocarditis and septic arthritis is still in a very unsatisfactory state, but we do know that streptococci, staphylococci, pneumococci and gonococci are very commonly associated with these lesions and that usually the local foci of infection through which these septic germs entered the body can be found.

I think there can be little doubt but that the cases of endocarditis above briefly referred to were septic from the start, and that if subsequent infection could have been avoided the period of apparent convalescence which all of these cases enjoyed might have been prolonged into a permanent recovery.

If the term *rheumatic* endocarditis be confined to those cases produced by the poison of true rheumatism and the term septic endocarditis be used to include all those cases following local foci of septic infection in the tonsils, lungs, pelvis and subcutaneous tissues, such as are produced by streptococci, staphylococci, pneumococci and gonococci, then it must be admitted that septic endocarditis is a very common affection and that the prognosis, while not as good as that of rheumatic endocarditis, is not necessarily

had provided second and third attacks can be prevented by medical and surgical measures looking to the destruction of local foci of infection and to the closing of the portals through which these poisons commonly enter the body.

The term *ulcerative* endocarditis has been very generally used as a synonym of septic endocarditis while, in fact, it should be used to describe those cases of septic endocarditis in which ulcerative changes occur in the endocardium, commonly on the valves. When this complication occurs we have a new and far more dangerous focus of infection in the very heart of the blood stream itself, from which the septic material may be distributed to every part of the body, producing a more general septicopyemia and in the vast majority of instances causing the death of the patient. It seems probable from the clinical history of these cases that ulcerations of the endocardium occur much more commonly in second and third attacks than they do in the primary attacks of septic endocarditis. It is also true that one attack of septic endocarditis may prepare the way for second attacks by storing up in the tonsils and other lymphatic tissues the spore or latent form of the germ or germs that produced the first attack, and when these second or third attacks occur, through a new infection or the lighting up of the old, it finds the damaged heart less able to withstand its onslaught, and an ulcerative endocarditis and fatal septicopyemia may result.

The rheumatic type of endocarditis is quite as distinct from the septic type as the rheumatic type of arthritis (true rheumatism) is from the septic type of this affection. It is possible, of course, that a rheumatic arthritis or endocarditis may be accidentally complicated by a septic arthritis, or endocarditis, but accidents of this kind do not vitiate the fact that the rheumatic and septic infections, although they may produce very similar syndromes are absolutely distinct and in no way related the one to the other.

The following case referred to in the opening paragraph is a good example of a septic endocarditis which later became ulcerative:

A. V. Patient was admitted February 10, 1905, to scarlet fever annex of the Cincinnati Hospital suffering from a moderately severe attack of scarlet fever. There was a previous history of pertussis and repeated attacks of severe tonsillitis. During the attack of scarlet fever the child suffered severely from sore throat

and a non-suppurative adenitis involving the cervical glands, especially on the left side. About the fifth day an endocarditis was discovered, which ran a moderately severe course, resulting in cardiac hypertrophy and permanent injury to the mitral valve. At no time did the urine contain albumin or casts.

On March 17, thirty-five days after entering the hospital, the patient was transferred to the Children's Ward. At this time there were slight fluctuations in the temperature, which were thought to be due to the adenitis. The heart was slightly enlarged and there was a systolic murmur at the apex transmitted outward, but there were no signs of cardiac distress or other evidence of acute disease of the heart. The temperature soon became normal, the cervical glands were gradually reduced in size, and the child's general condition steadily improved, until on April 20, sixty-eight days after entering the hospital, when convalescence seemed established, he was sent back to the Children's Home in a fairly good condition.

April 26. Six days later the child was returned to the hospital with a temperature of 103.5° F. and severe ulcerative tonsillitis. The Children's Home reported that the child has remained apparently well for five days after leaving the hospital and yesterday was taken acutely ill with fever and sore throat. The patient at this time presented the appearance of a fairly well-developed child and an examination revealed that he was suffering from a severe ulcerative stomatitis in addition to the tonsillitis referred to. The cervical glands were again very much enlarged and the left side of the face was swollen from an ulcer on the mucous membrane of the cheek that had been started by a ragged tooth. The systolic murmur at the apex was louder and rougher; the heart action was slightly irregular, its dulness was increased, and palpation revealed a thrill at the apex. The liver was slightly enlarged; the gastrointestinal canal was normal; the breath was very foul; there was a slight cough with possibly slight respiratory embarrassment; the urine was amber, specific gravity 1.018, acid in reaction, no albumin, casts or sugar.

It was apparent from the history and from the child's present condition that he was suffering from a new infection which had entered through the tonsils and produced systemic intoxication and a second attack of endocarditis.

The treatment ordered embraced a cathartic, rest, quiet, fluid

diet, small doses of whiskey and antiseptic washes for the mouth and throat.

May 1. During the five days the child has been in the hospital his temperature has been septic in type, varying from 104° F. to subnormal; the tonsillitis and stomatitis have improved; the cardiac condition, however, is worse as shown by the embarrassment to respiration, the increase in roughness of the cardaic murmur, the irregular rhythm of the heart and the diffusion of the apex beat.

May 13. The tonsillitis has disappeared, but the stomatitis and ulceration on the inside of the left cheek still continue giving a very fetid odor to the breath. During the last twelve days the liver and spleen have gradually increased in size until the liver extends half way to the superior spine of the ilium, and the spleen extends below the level of the umbilicus. The enlargement of these organs produces a marked prominence of the upper half of the abdomen. There is also general lymphatic enlargement, especially of the cervical nodes, a chain of these enlarged nodes extending anteriorly and posteriorly from large lymphatic masses below the ears, completely girdling the neck. These lymph nodes vary in size from a pea to a walnut, the largest being under the angles of the jaw. The posterior part of this lymphatic ring extends around the back of the head reaching at its highest point the occipital protuberance and running from this point to the angle of the jaw on either side. The lymphatic enlargements in the groins and axillæ are very noticeable, and it is worthy of note that while this lymphatic enlargement is general it is more marked throughout on the left side of the body.

The patient is gradually losing weight and strength; his temperature, while not running quite so high, is still septic in type; the action of the heart has slightly improved, but his anemia has increased until the child's pallor is now very noticeable; the face has a sallow hue, the mucous membranes of the lips and conjunctiva are pale, the appetite and digestion are poor, but he has as yet shown no hemorrhagic tendencies.

May 15. Bacteriological examination of the blood made on May 13th was negative. A blood count showed marked anemia with 41,000 white cells. Differential count gave the following result:—Polymorphonuclear neutrophiles, 62 per cent; small

lymphocytes, 24 per cent; large lymphocytes, 8 per cent; eosinophiles, 4 per cent.

The previous and subsequent history of this case might suggest that the failure to find microorganisms in the blood may have been due to an error in technique; the examination, however, was made by an experienced bacteriologist.

During the past two days the patient has developed a fine purpuric rash over the whole body, and the discharges from the bowels have contained some blood and mucus.

May 18. The temperature is still septic in character, and is now reaching a daily maximum of 104° F.; the urine continues negative; the lymphatic nodes, heart, liver and spleen remain much the same; the ankle, knee, and hip-joints have become tender and swollen, so that the child lies with his legs flexed and cries with pain when an attempt is made to straighten them; the purpuric rash is fading; the gums remain very sore and tender and bleed readily on pressure.

May 29. The temperature during the last seven days has been normal. The chain of nodes extending around the back of the head are filled with pus; these abscesses were opened. The child's general condition is much improved; the spleen has gradually been reduced in size until now it can be felt just below the margin of the ribs; the liver is also now but slightly enlarged; the heart's action is regular; there is no evidence of cardiac distress, the systolic murmur is not so rough and loud, and the apex beat is more clearly defined.

The patient continued to improve, the temperature remaining normal until June 5, when suddenly it mounted to 102.5° F. This was followed by redness of the conjunctiva, coryza and the bronchitis, and the child's general condition also became much worse. On June 7 a well-developed measles rash appeared, and the patient was transferred to the measles ward. At this time the stomatitis, which had continued, became very much worse, and the ulceration on the inside of the left check had spread to such an extent that the whole cheek was swollen and a distinct area of tumefaction was developed.

The measles rash remained out for three or four days, and during this time a bronchopneumonia and enteritis developed. The temperature remained high and irregular, and the ulceration

in the inner side of the left cheek continued to increase in size, so that on June 20 the mucous membrane surrounding the ulcer was gangrenous, and it was evident that cancrum oris had developed. On June 24 the gangrenous ulcer perforated the cheek, making an opening large enough for the insertion of a finger. This slough gradually increased in size, the enteritis and bronchitis continued with high and irregular temperature until the 28th, when the child died.

Necropsy was made four hours after death. The heart was enlarged; pericardium contained an excess of fluid; heart muscle was hypertrophied and firm; the mitral valve had an ulcer on both leaflets; the spleen was enlarged, congested, soft and pulpy; kidneys cloudy, pale and swollen, capsule strips easily; liver enlarged, but contained no metastatic abscesses. The lungs showed a well-marked bronchopneumonia. The left cheek was perforated by a large gangrenous ulcer.

GONOCOCCIC VULVOVAGINITIS IN YOUNG GIRLS. (Revista Española de Pediatriá, Zaragoza, 6: 820, Nov.-Dec. 1950). Carrera reports that 75% of the cases of vulvovaginitis are of gonococcic origin. The incidence of the disease in the newborn is not high because of maternal hormonal protection; it occurs much more frequently later in childhood. The disease tends toward spontaneous cure and always disappears before puberty. The author points out the ineffectiveness of treatment with irrigations, ointments, washings, and fever therapy. Although estrogen therapy produces temporary relief the dangers that accompany its use, i. e., congestion of the mammary glands, development of secondary sex characteristics, colic, and possible cancerigenic action prohibit its extensive use. Sulfonamide therapy effected a 55% cure rate; combined sulfonamide and estrogen therapy was more effective. Penicillin was more effective than sulfonamides, without the toxic effects of the latter. Streptomycin administered up to a total dose of 5 gm. furnished the best results, since it acts on all the bacilli involved, including gonococci and streptococci. The author concludes that streptomycin is always indicated in the treatment of vulvovaginitis in young girls whether gonococci enter into its etiology or not.—*Journal A.M.A.*

DEPARTMENT OF ABSTRACTS

Orr, W. W.; Preisser, W. G.; Ross, S.; Burke, F. G. and Rice, E. C.: Evaluation of Intravenous Chloramphenicol. A Preliminary Report. (Antibiotics & Chemotherapy, 1:63, April 1951).

Preliminary studies of the intravenous method of administration of chloramphenicol employing acetyl-dimethylamine as the solvent indicate that the drug may be given rapidly as a 1 per cent solution in a diluent, such as 5 per cent glucose in water, in therapeutic doses in children without any untoward reactions. A dose of 15 mg. per Kg. every 6 hours is recommended. Intravenous administration of the drug would be indicated in severe infections where the patient is semicomatose or unable to take the medication by mouth. Further studies on the toxicity of parenteral chloramphenicol are indicated before the preparation is employed on a widespread scale. Authors' Summary.

Asher, P. and Schonell, F. E.: A Survey of 400 Cases of Cerebral Palsy in Childhood. (Archives of Disease in Childhood, 25: 360, Dec. 1950).

The authors report on their survey of 400 cases of cerebral palsy 349 of which were of the congenital type and 51 of which were acquired cerebral palsy. Among the 349 cases of congenital cerebral palsy there were 290 cases of spastic paralysis, 36 athetoids, 17 mixed cases, 3 cases of ataxia, 2 of flaccid paralysis and one of rigidity and tremor. Evidence from this series suggests that athetosis is usually the result of birth injury or asphyxia or neonatal jaundice, whether due to Rh iso-immunization or not. Birth injury probably causes some cases of spastic paralysis, while others are the result of genetic or intrauterine factors. Fifty-one cases of acquired cerebral palsy were examined. These comprised 19 cases of kernicterus, 14 of acute infantile hemiplegia, 11 postmeningitis palsies, 2 other infective cases, 4 cases of progressive spastic paralysis and 1 of posttraumatic hemiplegia.

The I.Q. was 70 or over in 51 per cent of the cases, between 50 and 69 in 23 per cent and below 50 in 26 per cent. No significant difference in the mean I.Q. of spastics and athetoids was found. The mean I.Q. of the various groups varied inversely with

the severity of the physical handicap. An examination of the attainment in reading of the normally intelligent and bright children reveals a considerable degree of retardation. This suggests, that, unless special educational provision is made, many cases will lack the stimulus necessary to develop their capacities beyond mediocre levels. MICHAEL A. BRESCIA, M.D.

ADAMS, F. H.; BERGLUND, E.; BALKIN, S. G. AND CHISHOLM, T.: PITUITARY ADRENOCORTICOTROPIC HORMONE IN SEVERELY BURNED CHILDREN. (Journal American Medical Association, 146: 31, May 5, 1951).

Administration of ACTH to severely burned children is a rational form of treatment, justifying further investigation. The hormone has been given to three patients (ages 4 to 11 years) who had severe burns of the body. One of the patients received the hormone for five days and two received the hormone for 30 and 100 days, respectively. Administration of the substance produced a decrease in fever, an increase in the caloric intake and an improvement in the emotional status of the patients. Its administration to the three patients did not interfere with wound healing or the take of the skin grafts. AUTHORS' SUMMARY.

RICH, A. R.; COCHRAN, T. H. AND MCGOON, D. C.: MARKED LIPEMIA RESULTING FROM THE ADMINISTRATION OF CORTISONE. (Bulletin Johns Hopkins Hospital, 88: 101, Jan. 1951).

The daily administration of 7.5 mgm. of cortisone to normal adult rabbits kept on a balanced stock diet produces a marked degree of lipemia, with a rise in both the total fatty acids and total cholesterol of the serum, and striking deposits of visible fat in the liver. There is no constant parallelism between the degree of lipemia and the degree of glycosuria. AUTHORS' SUMMARY.

DAVIDSON, H. H.; HILL, J. H. AND EASTMAN, N. J.: PENICILLIN IN THE PROPHYLAXIS OF OPHTHALMIA NEONATORUM. (Journal American Medical Association, 145: 1052, April 7, 1951).

In 9,241 consecutive newborn treated with penicillin intramuscularly as a prophylaxis against gonorrheal ophthalmia, not a single case of the disease developed. In an additional 4,163 consecutive newborn in whom penicillin ointment (7,000 U.), intra-

muscular injection of penicillin (10,000 U.) or silver nitrate (1 per cent) was used in weekly rotation, one or more signs of local irritation (redness, edema or discharge) developed in 10.6 per cent of the penicillin ointment series, in 13.8 per cent of the intramuscular penicillin series and in 48.7 per cent of the silver nitrate series. The authors feel that the penicillin ointment is the most efficacious, the safest and the least irritating agent for the prophylaxis of gonorrheal ophthalmia. In addition, it is easy to instill into the conjunctival sac and economical.

MICHAEL A. BRESCIA, M.D.

IRVING, F. C.: MEDICINE AS A SCIENCE—OBSTETRICS. (New England Journal of Medicine, 244: 91, Jan. 18, 1951).

The author discusses the advances accomplished in the field of obstetrics during the last 50 years. In the course of the discussion, Irving had the following to say anent the newborn. Breast feeding has deteriorated in the last 50 years to a marked degree; in fact this is the only respect in which obstetrics has gone backward. There is evidence that infants so nourished gain more rapidly and are more resistant to disease; moreover, it encourages sociability, for Plutarch says of it that "constant feeding together is a great means to heighten the affection mutually betwixt any persons." The disinclination of many recent mothers to nurse their babies arises from many causes, but is fostered by the safety of substitute feedings—a safety not due to any pediatric magic but to the fact that most cow's milk fed to infants is pasteurized. Recently, a group of persons have appeared who are known as child psychologists. They maintain that a newborn infant should not be nursed at regular intervals but whenever it cries; otherwise, they say, it will suffer in later life a sense of frustration. How they know this they do not say. The characteristics of many American children, however, lead one to wish that there had been more instead of less family discipline, and that it had begun at the earliest possible age. MICHAEL A. BRESCIA, M.D.

BURROWS, N. F. E.; RENDLE-SHORT, J., AND HANNA, D.: LEAD POISONING IN CHILDREN. REPORT OF FIVE CASES, WITH SPECIAL REFERENCE TO PICA. (British Medical Journal, 4702:329, Feb. 17, 1951).

The authors present 5 cases of lead poisoning in children ranging in age from 5½ months to 7 years. Four of the cases were associated with pica, and in the case of the infant of 5½ months was caused by the use of a lead shield for 10 weeks. One of the patients died (a girl of 1 year and 7 months) and two appear to be mentally retarded. The sources of the lead can be broadly divided according to the age group: (1) In infancy due to lead nipple-shields, or lead-containing powders. (2) Between 1-5 years due to children with pica eating lead along with other noxious substances, most often in the form of lead paint. (3) School children due to accidents similar to those met with in adult life. The manifestations in childhood differ from those in adults in that encephalopathy, with irritability, fits and coma is very common. Wrist-drop and the lead line on the gums, however, are rare. The diagnosis is often first suspected from the finding of punctate basophilia in a blood film. Although not diagnostic, punctate basophilia should lead to further investigations, of which x-ray examination of the long bones is the most important. Lead poisoning in children is a preventable disease. MICHAEL A. BRESCIA, M.D.

MEAD, C. I.: COCCIDIOIDOMYCOSIS IN CHILDREN. (Journal American Medical Association, 146:85, May 12, 1951).

Coccidioidomycosis is a definite pediatric problem in the southwestern U. S., especially during vacation periods from school when travel is more general. As the children grow to adulthood, coccidioidomycosis in endemic areas becomes less of a problem because in a large part of the population immunity develops. Once a child has had the disease and recovered, an immunity has been established and reinfections do not occur. Recent work seems to indicate that maternal infections in the first trimester do not cause anomalies in the infant, while infections in the last trimester are a greater hazard to the mother and more often result in premature birth of the infant. The infection in the colored race carries greater hazard of dissemination than in the white race. If infection has occurred, it is of no value to move from the endemic area. Rest alone is the best treatment. The temperature chart and sedimentation rate will give the best clue as to when the disease becomes arrested. MICHAEL A. BRESCIA, M.D.

VIDEBAEK, A.: MALIGNANT TUMORS IN CHILDHOOD. (Acta Paediatrica, 39:502, 1950).

Childhood malignancy is nearly always of mesenchymal origin, epithelial growths (carcinoma) occurring very rarely. Any organ and any tissue in the child appears to be able to form a neoplasm. In children, as in adults, malignant growths may arise in any region, and since childhood growths arise mainly from interstitial tissue, their localization is even less consistent than in adults, whose new growths are so often epithelial and therefore commonly encountered in certain organs or systems. The incidence of malignant disease in childhood is about 1-2 cases per 10,000 children. The lowest incidence of cancer in both sexes is in prepuberty, about the seventh year. Actual childhood tumors occur before this age and are predominantly sarcoma and mixed tumors. Two hundred seventy-six cases of malignancy in children under 15 years of age were reported to the Danish Cancer Registry for the years 1942-1944. These included 84 cases of Hodgkin's disease, leukemia and myeloma, 56 cases of sarcoma, 54 brain tumors, 11 skin carcinoma, 11 renal tumors, 5 cancers of the digestive tract, 4 abdominal cancers, 4 cancers of the male genitalia and 2 of the female genitalia and 45 miscellaneous cancers.

MICHAEL A. BRESCIA, M.D.

WALLGREN, A.: THE UNDERGRADUATE TEACHING OF PEDIATRICS. (Acta Paediatrica, 39:524, 1950).

The increasing importance of child health makes a revision of pediatrics in the medical curriculum necessary. Pediatrics should be made one of the main clinical subjects, and the teaching of pediatrics should be effective enough to guarantee satisfactory practical knowledge of the healthy and sick child. The importance of the selection of the teachers and the students, restriction of the number of accepted students, organization of the teaching program and better technique of the teaching is stressed. The individual bedside training in the wards or at the out-patient department should be more emphasized. The collective teaching in the classroom should only be a minor part of the program and be improved by the introduction of new methods aiming at a more active participation of the audience. The length of the pediatric curriculum should be preferably not less than 3 months, the optimal time probably

being 5 months, including clerkship or internship. The course should be postponed until the end of the clinical undergraduate studies and terminated by an examination.

AUTHOR'S SUMMARY.

DOXIADIS, S. A.; EMERY, J. L., AND STEWART, S. M.: ORAL PENICILLIN IN CHILDREN. (British Medical Journal, 4696:16, Jan. 6, 1951).

Seventy-six children, aged 2-15 years, were given penicillin two or more hours after a light breakfast. It was in tablet form, each containing 200,000 units. The dose given varied from 1,000 to 7,000 U. per pound of body weight. Sodium citrate was used as an antacid. It was given immediately before or after the penicillin. To attain a reliable bacteriostatic level of 0.06 U. per ml. three hours after the ingestion, the single dose of penicillin should be not smaller that 6,000 U. per pound of body weight—that is 48,000 U. per pound of body weight in 24 hours. Simultaneous administration of an antacid may allow a reduction of this dose by approximately 50 per cent. MICHAEL A. BRESCIA, M.D.

HOLZEL, A.: HYPERTRICHOSIS IN CHILDHOOD. A CLINICAL STUDY. (Acta Paediatrica, 40:59, Jan. 1951).

Physiologically lanugo covers the body of the premature to a large extent, but occasionally it is found on the limbs and shoulders of the full term. The lanugo covering persists for several weeks and is then gradually lost. Between 3 and 6 years of age a large number of children, irrespective of their hair color and sex, show transitional hair growth of a fairly constant distribution similar to that of the adult. At school age, however, this hair distribution is less frequently seen and hair growth is found on the body mainly localized in the interscapular area spreading occasionally to the skin over the scapulae. Sometimes interscapular and limb hair growth occur together. Transitional hair is replaced after puberty by the final hair of the adult. The author has classified hypertrichosis into two groups, primary on a congenital or familial basis and the secondary or transient type. The latter type is associated with endocrine disorders, acrodynia, celiac disease, hematogenous forms of tuberculosis and marasmus.

MICHAEL A. BRESCIA, M.D.

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